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CONTENTS

CLINIC OF DR. DAVID RIESMAN

Philadelphia General Hospital

UNUSUALLY DISTENDED BLADDER SIMULATING ASCITES

THE first case I am going to speak about is that of a man I did not see in life and now he is no longer with us. The dead often teach us lessons as valuable as the living. What can our departed patient, Alexander Johnson, teach us? He was a colored man, sixty-eight years of age, admitted to the hospital on Saturday, October 5th, complaining of shortness of breath and "swollen stomach." He was seen by Dr. Head who ascertained that he had been well until two years ago. At that time he was told that he had a tumor and should have an operation. He did not know what kind of a tumor he had or where it was situated, but it evidently did not incommode him very much for he declined operation and kept on with his work as a waiter. Lately he had become a little short of breath, was moderately troubled with nocturia, and had noticed progressive enlargement of his abdomen. Physical examination revealed a rather large heart, a systolic blood pressure of 230, a diastolic pressure of 110, and a marked abdominal enlargement extending up to the umbilicus. The swelling gave a fluid wave, i.e., it fluctuated and seemed to change with change of posture. On Sunday, October 6th, Dr. Head was away from the hospital, when she saw the patient again on Monday morning he was gravely ill and died in a few hours.

From the history and the findings in this patient, as I have related them to you, I doubt whether you could make a correct diagnosis   Those who saw him thought that he had ascites, probably of cardiac origin   What were the findings at autopsy? The pathologist found a bladder, filled with urine, extending up beyond the umbilicus   The bladder which I now show you is very much shrunken because of the preservative, but it is still of extraordinary size and is marked by numerous criss-cross trabeculæ   The prostate you will note is as big as a grapefruit   I do not remember ever seeing a larger one   You will also observe that the ureters are dilated, and that there is a pronounced hydronephrosis   I shall pass the specimen around as I want all the students to see it   It is most interesting that this patient had no urinary symptoms of moment and was going about his daily work until shortly before his admission   The history, it is true, tells us that several years ago he was told that he had a tumor, it is a reasonable supposition that that statement referred to the enlarged prostate   It may also be that it had reference to the abdominal enlargement produced by an over-filled bladder   No one knows

For comparison Dr Head has brought another bladder, more normal in size, but with thickened trabeculated walls and beginning prostatic hypertrophy

What lesson does this case teach us?   Several   It reminds me of an incident many years ago when I was sitting, as you are today, a student on the benches   In those far off days the medical man seldom did tapping of the abdomen, he usually referred the cases requiring this procedure to the surgeon   At the present day   the surgeon graciously allows him to do this   We were gathered at a clinic given by the late Dr Ashhurst   From the Medical Service a man had been sent down to the Surgical Clinic with the diagnosis of ascites and the request that he be tapped   Dr Ashhurst, who was, I think, the keenest diagnostician of his period not only surgically but also in those borderline cases between surgery and medicine, after reading the history of the patient, with the diagnosis of ascites and the request for tapping   turned to his assistant and said   "Will you please

bring me a catheter?" He used the catheter and the ascites disappeared I distinctly remember there were present some of the medical men who had studied the patient and we were witnesses of their comprehensible discomfiture This mistake was made in the last century but it will be made many times in this one How can it be avoided? By forming what I might call the "bladder habit" in examining patients, i e, the habit of examining the bladder in all cases that remotely make a diagnosis of retention of urine possible During the great influenza epidemic in 1918 I was frequently struck by a curious restlessness of gravely ill patients I found quite early that this restlessness was often due to an acutely distended bladder My first impulse on examining patients was to percuss the bladder region and many a time I was able to relieve the restlessness, which no sedative had been able to control Once the bladder was emptied, the patient would become quiet and often would go to sleep In typhoid fever, pneumonia, and septicemia, after labor and after an operation, in patients who have apoplexy, the bladder may not be properly emptied The patient may then exhibit an ill-defined discomfort which cannot be relieved unless the bladder is emptied Do not let the statement of the nurse that the patient is voiding freely and is soaking the bed sheets mislead you, for notwithstanding this, the bladder may be full to bursting

I recall several other interesting cases that I might speak of in this connection One of the most remarkable was in this hospital several years ago A colored man had come in complaining of abdominal pain and as he was a painter, the process of reasoning naturally was "painter, paint, pain, lead poisoning" I examined the patient, a young man not over twenty-five years, and found no blue line present, the only thing of moment was a tumor of the abdomen extending up to the umbilicus He was catheterized and the tumor disappeared He left the hospital the next day cured of his "lead poisoning" It is hard to explain this retention I remember asking that particular patient about it and he said he did not know his bladder was full The other day a young neurasthenic individual of

twenty-five came to my office complaining of nothing in particular On examination I found a swelling extending up nearly to the umbilicus I asked him whether he had passed water recently and when he said no, I instructed him to empty his bladder He emptied the tumor The etiology of such curious conditions is obscure, it may be that there is a nervous reflex, sometimes there has been an excessive intake of water in persons with a tight vesical sphincter or a high reflex threshold

ACUTE GASTRO-ENTEROCOLITIS WITH HIGH NITRO-GEN RETENTION IN THE BLOOD, PARATYPHOID A INFECTION, FOOD POISONING

The patient I now show you is a very nice fellow in whom and in whose disease we have all been deeply interested The present ward class knows this man, whose name is William Frazier, forty nine years old, a chauffeur by occupation I shall give you the important points in his history About the middle of September he had some moonshine whiskey of which he drank a liberal amount A few days later he ate a quantity of water cress and raw tomatoes and drank water from a well in the out-skirts of West Philadelphia He was all right the next day, but on the following day he vomited and had a profuse diarrhea with a good deal of abdominal pain and tenesmus He says that he passed a large amount of mucus, but did not notice any blood in the stools When questioned as to how many times his bowels had moved, he said he had to stay in the woods all day to attend to his rectal needs, and he thinks he had at least fifty movements We had a patient here in this hospital with a similar condition and I had the nurses keep account of his evacuations—the record was forty nine movements in twenty four hours This patient says he had fifty but he has not kept as accurate a tally as our nurses On admission he appeared to be very much emaciated, the skin and mucous membranes were dry, the impression he gave was one of semi shock He had a good deal of abdominal pain and tenesmus The bowel movements contained mucus, but no blood The blood pressure was 75 systolic and 60 dias tolic, almost the blood pressure of shock The stools were ex amined on five different occasions and invariably found to con tain Bacillus paratyphosus A Another interesting feature was revealed when the blood chemistry was studied This showed urea nitrogen 95 mgm per 100 c c of blood at the first examina

tion, and 125 mgm a few days later   Dr Head has placed on the blackboard the results of the chemistry studies   For comparison I have had her put down the normal findings as given by MacLeod in his famous text-book

BLOOD CHEMISTRY

	Urea N	Creatinin	CO₂	Sugar	Cholesterol.	NaCl.	N P.N	Uric Acid
Normal	12–15	1–2	50–75	90–120	0 14– 0 17%	0 57– 0 62	25–30	2–3
9/30	95	5 7	38	111				
10/1	125	5 2						
10/5	20		60	126				

Blood-count

	R.B C	W B C	Hg	Polys	Lymph	Trans	Eosin	Bas
9/27/29	4,410,000	5400	16 1	36	58	2	2	2

The Widal test was negative

You will observe that the urea nitrogen is very high   The creatinin is almost twice the normal   Seeing these figures, what would you say ailed such a patient?

ANSWER—Student   Nephritis

Yes, I think it would be the diagnosis made by many   Let us see the report of the urinary findings   Specific gravity, 1 013 to 1 015, albumin from traces to a light cloud, on microscopic examination, many hyaline and occasional granular casts   Taking these data of the blood chemistry and urine together, we might consider the diagnosis of nephritis not only tenable but almost imperative   We might even conclude that the dysenteric symptoms were an expression of uremia, for it is well-known since the days of the English clinician, Dickinson, that in the terminal stages of Bright's disease an ulcerative colitis may develop   Such patients are extremely toxic   Our patient, while he looked ill and "verfallen," as the Germans say, did not seem toxic or in the terminal stages of uremia   This, together with the fact that the man had been well until a short time before, made me unwilling to consider the case one of nephritis   I was of the opinion that he had an acute colitis or gastroenterocolitis or dysentery due to some form of food poisoning

If he did not have chronic Bright's disease, you are no doubt asking what is the cause of the great nitrogen retention. I refer the question back to you.

ANSWER—Student Dehydration

Yes, that to my mind is a reasonable explanation in this case. Not only did our patient loose large quantities of fluid by vomiting and excessive purgation, but during the acute period of his illness he took no food and no fluid and in consequence his tissues were desiccated. We are beginning to learn a little about water metabolism and its great importance to the body. A proper water balance is necessary for the maintenance of the acid base equilibrium and for proper elimination on the part of the kidneys and the skin. I would recommend to your attention in this connection an interesting article by J B S Haldane in his recent book "Possible Worlds."

We cannot form a satisfactory estimate of the part played by the kidneys in the nitrogen retention in our patient. The urine findings indicated a change in the renal structure. It could scarcely have been a true nephritis for the urine cleared up in the course of a few days. I would ascribe the renal changes to toxic substances generated in the intestinal tract, which the kidneys attempted to eliminate. Whether the dehydration as such, with the consequent altered chemical composition of the blood, played any part in the pathogenesis of the renal changes it is difficult to say. It seems there is a vicious circle—a toxic irritation of the kidneys may lead to retention of waste products in the blood, and the passage through the kidneys of such concentrated blood may in turn act as an irritant to the renal cells and the blood vessels.

The literature on dehydration and its effects, especially on the blood chemistry is very meager. I have given only a cursory glance, but it revealed nothing of value. What was our plan of treatment? On the assumption that dehydration was largely responsible for the symptoms we administered large amounts of fluid, in the form of glucose and saline solution, 5000 c c subcutaneously and 1000 c c intravenously. In consequence or at least soon thereafter, the patient's urea nitro

gen fell from 125 to 20 and the blood-pressure rose to 126 systolic and 78 diastolic, the latter higher than the systolic had been previously The urine also became normal In addition to the large amount of fluids we administered a little bismuth for the colitis, and the bowels now appear to be normal We shall let William Frazier go home as soon as he has had three negative feces cultures He promises forever to abstain from moonshine whiskey and I know he will keep his promise

Before I pass to another interesting feature of this case, I want to emphasize one of the salient points emerging from our study, viz , that one cannot depend too much upon laboratory tests They must always be interpreted in the light of the clinical findings and the history And now I want to say something about the cause of this man's dysentery As we have no sample of the moonshine whiskey, nor of the watercress and tomatoes, nor of the well water, we are unable to test them and therefore are in no position to incriminate definitely any one of these substances Formerly, Frazier's case would have been diagnosed as one of ptomain poisoning, but the more the subject of food poisoning is studied the less important become ptomains in the etiology To quote Jordan (Porto Rico Review of Public Health and Tropical Medicine, May, 1929), "While the diagnosis of ptomain poisoning has its uses as a convenient refuge from etiologic uncertainty, it can hardly serve as a precise designation of an actual pathologic event The majority of the carefully investigated outbreaks of acute gastro-intestinal disturbance of the type that at one time were denominated ptomain poisoning are now found to be associated with the presence of bacilli of the paratyphoid group "

Several forms of so-called food poisoning are really not food poisoning, as, for example the poisoning resulting from eating toxic mushrooms, especially the deadly anamita, and other plants The substances eaten are not foods Another form somewhat akin is the poisoning that comes from eating honey derived from blossoms of azalea and rhododendron and other plants

On account of its great historical interest I shall quote a

paragraph from Xenephon's Anabasis which I find in Dr Jordan's article mentioned above Dr Jordan's attention had been called to it by Dr McCollum

"After accomplishing the ascent the Greeks took up quarters in numerous villages, which contained provisions in abundance Now for the most part there was nothing here which they really found strange, but the swarms of bees in the neighborhood were numerous, and the soldiers who ate of the honey all went off their heads, and suffered from vomiting and diarrhea, and not one of them could stand up, but those who had eaten a little were like people exceedingly drunk, while those who had eaten a great deal seemed like crazy, or even, in some cases, dying men So they lay there in great numbers as though the army had suffered a defeat, and great despondency prevailed On the next day, however, no one had died, and at approximately the same hour as they had eaten the honey they began to come to their senses, and on the third or fourth day they got up as if from a drugging "

Food poisoning following soon after the partaking of the usual articles of diet may be due to the intentional admixture of a mineral poison, such as arsenic This Borgian method of getting rid of an undesirable rival or husband is no longer common, but I remember a famous case of this sort which happened in Philadelphia a number of years ago Slower forms of arsenic or lead poisoning have been traced to food or drink contaminated with one or the other of these poisons Some food poisonings may be due to the improper addition of food preservatives I have seen a whole family made ill by alum in baking powder, fortunately, they all recovered

The majority of genuine food poisonings are due to bacteria and their products Typhoid fever may be a food poisoning especially in the outbreaks due to typhoid carriers The more typical cases of food poisoning have arisen as local outbreaks following the ingestion of contaminated meat or meat products and have been traced to special groups of bacteria which are sometimes loosely called paratyphoid bacilli The first thoroughly studied outbreak occurred in a small German village in 1888

and was found by Gartner to have been caused by the use of
meat from a cow slaughtered because it was ill with a severe
enteritis   Gartner isolated a micro-organism which he called
Bacillus enteritidis   The majority of meat poisonings since then
have been traced to one of two species of organisms, either the
Bacillus enteritidis of Gartner or the B aertrycke   The latter is
similar to but not identical with Bacillus paratyphosus B

At times the symptoms of gastro-enteritis come on so quickly
after the ingestion of contaminated food that bacteria could
hardly have had time to pullulate in the body and we must as-
sume that soluble poisons or toxins were present in the contam-
inated article   That such soluble toxins do actually occur in poi-
sonous food is illustrated by that most interesting and most
pathetic of all forms of food poisoning, namely, botulism   The
name botulism, or sausage poisoning, is not strictly appropriate
because although some of the earlier outbreaks were traceable
to sausage meat, the majority of recent cases have been due to
canned vegetables—corn, string beans, asparagus, and spinach
The cause of botulism is the Clostridium botulinum   Like the
tetanus and the diphtheria bacillus, it produces a powerful
soluble toxin or exotoxin

Unlike the paratyphoid organisms and their allies which
cause gastro-enteritis, the botulism bacillus produces _nervous
symptoms, particularly disturbances of vision and of swallowing
The symptoms in the beginning are not unlike those of lethargic
encephalitis

I might relate an interesting story of an outbreak of para-
typhoid or typhoid fever in one of the cities in this state   A
department store had imported a large number of parrots for
sale at Christmas   About the same time an outbreak of an ob-
scure fever occurred, which some of the doctors called para-
typhoid fever   This to the laity sounded like "parrot typhoid
fever," and they naturally ascribed the disease to the parrots
There is a disease conveyed by parrots, viz , psittacosis, it is
due to the Bacillus psittacosis, but usually takes the form of
pneumonia and not of gastro-enteritis

I would recommend to you to read Jordan's Bacteriology

and his excellent article in the Porto Rico Review already quoted for a very clear account of the subject of food poisoning

To return once more to our friend William Frazier, we find in his history that at the age of seven he had a "touch of typhoid fever" "Touch" may mean anything, but one might not un reasonably think of the possibility that he had paratyphoid fever then and is a carrier now The possibility is very remote, however, and we shall see in a few days whether, as I expect, the paratyphoid bacillus will not have disappeared from the stools, for I am inclined to the opinion that his gastro-enterocolitis was an acute condition brought on by paratyphoid organisms ingested with the watercress or drinking water, and that they will promptly disappear from his excreta [1]

[1] Stools were positive for Bacillus paratyphosus A on 9/27 9/28 9/29 10/1 and 10/3

They were negative on 10/8 10/11 and 10/16

The urine was at all times free from paratyphoid bacillus

CLINIC OF DR. GEORGE MORRIS PIERSOL

FROM THE DEPARTMENT OF INTERNAL MEDICINE OF THE GRADUATE
SCHOOL OF MEDICINE OF THE UNIVERSITY OF PENNSYLVANIA,
AND THE MEDICAL SERVICE OF THE PRESBYTERIAN HOSPITAL OF
PHILADELPHIA

SPORADIC TYPHUS FEVER (BRILL'S DISEASE)

THE term "typhus fever" invariably calls to mind that
severe, acute infectious disease which from earliest times has
proved one of the great epidemic diseases of the world. It de-
velops in overcrowded cities, in prisons, camps and even in
hospitals, in short, wherever large numbers of people are crowded
together under unsanitary conditions. Today, thanks to im-
proved sanitation and better living conditions, typhus fever, in
its severe epidemic form, is practically eliminated from this
country and from Western Europe. Endemic centers of typical
typhus still exist in Central Europe, Russia, Serbia, Northern
Africa, and in certain sections of China and in Mexico. During
the World War, devastating epidemics occurred in Serbia, and
the disease was wide-spread in Poland and Russia following
the war.

In 1910 Ricketts isolated an organism, Rickettsia prowazeki,
in lice infected with Mexican typhus. His observations were
subsequently confirmed by several observers. More recently
Wolbach, Todd, and Palfrey,[1] of the Red Cross Commission
for the study of typhus fever in Poland proved conclusively
that Rickettsia prowazeki is the cause of typhus fever and that
the disease is transmitted by the body louse. These etiologic
facts explain why the disease, in its epidemic form, has always
been prevalent where filth and overcrowding co-exist.

Since, as the result of improved living conditions, the severe
type of typhus fever is no longer a problem in our American
cities, we are prone to overlook the fact that in addition to

the classic devastating typhus, this disease also occurs
mild sporadic form which is by no means infrequent i:
cities of our Eastern Seaboard   The very existence of
mild form of typhus fever is often forgotten and undoub
the majority of these cases go unrecognized   For that r
it seems worth while to call your attention to this type c
infection

Nathan E Brill, of New York, became impressed wit'
fact that among the large number of typhoid fever pa'
which were under his care, there were certain cases w
although they clinically resembled typhoid fever in man
spects, were not identical with that condition and dic
give a positive Widal reaction   He first published his obs
tions in 1898 [2]   Some years later, in 1910, Brill[3] publishe
admirable clinical study based upon 221 cases of "an
infectious disease of unknown origin," which in some
resembled both typhoid and typhus, fever   Although h
mitted the greater similarity of his cases to typhus feve:
nevertheless, stated "I believe this disease not to be ty
fever "   Like many others, Brill's conception of typhus
was limited to the severe, fatal, highly contagious form o
disease

After Brill s observations many similar cases were rec
in the literature, which were soon referred to as "Brill's dise
Thirteen such cases were reported by Morris J Lewis a
Pennsylvania Hospital in 1911 [4]   The true identity of I
disease, however, was not established until 1912, when And
and Golderger' showed that monkeys were susceptible t
fection from blood taken from cases of Brill's disease,
further that monkeys recovered from Brill's disease coul(
be infected with Mexican typhus fever, and that the con
was equally true   These immunologic studies showed defir
that Brill's "infectious disease of unknown origin," was idei
with Mexican typhus fever   These observations have
amply confirmed, and there is no doubt that a mild spo
form of typhus fever is constantly present in the large citi
this and other countries   It is difficult to state the incic

of this typhus fever in our larger communities, since most of the cases are either unrecognized or erroneously diagnosed as typhoid fever

In 1912 Roger I Lee,[6] studying the cases in the Massachusetts General Hospital from 1902 to 1912, found a ratio of about 1 case of typhus fever to 47 of typhoid   Blumer[7] has personally observed 6 cases of typhus fever in and about New Haven in the past twenty years

Within the last few weeks we have had under observation in the medical wards of the Presbyterian Hospital, a case which clinically bears such a striking resemblance to the cases of mild typhus, so admirably described by Brill, that such a diagnosis seems justifiable

The patient is a machinist, born in Scotland, age twenty-six years, and single   He was admitted on September 13, 1929 complaining of fever, violent headache, and violent pains in the neck and back

Until three days before admission he stated that he was absolutely well   Upon September 10th while at work, he was seized with a sudden severe chill, which lasted ten minutes After this he was so prostrated that he had to give up work immediately and go to bed, where several other chills occurred Following the first severe chill he developed a violent frontal and occipital headache, associated with backache, insomnia, and high fever   Two days later he vomited   He was seen by his family physician and promptly referred to the hospital

He stated that he had never been subject to headaches and never had a severe headache before   There had been no disturbance of vision   There were no symptoms referable to the respiratory tract   Except for the vomiting, there were no gastro-intestinal symptoms   Since the onset of the disease he had been constipated   There were no symptoms referable to the genito-urinary tract

His previous medical history was of no significance   He never had had typhoid fever, or any severe acute infection, his tonsils had been removed during childhood and he had never suffered from any venereal disease

There was nothing of importance in the family history He had worked steadily at his trade for years, his personal habits were good, he used alcohol rarely, his living conditions were satisfactory and reasonably clean He denied any recent lousiness There was a history of possible recent exposure to typhoid fever which caused some diagnostic uncertainty

His physical examination on admission was as follows The patient was a well-developed and well-nourished young male adult His body was clean and showed no evidence of lice He was profoundly prostrated, apathetic, and looked ill His face was markedly flushed He complained constantly of severe pain in his head and in his neck The most striking feature of his examination was a generalized maculopapular eruption, most marked on the chest, abdomen, and back, but also involving to some extent his extremities There was, however, no eruption on the face The macules were irregular in shape and size Some of them were confluent They were dusky red in color and some had become slightly petechial They did not disappear on pressure and did not come out in crops The patient stated that this eruption began on the day following the chill His pupils were dilated, equal, and reacted normally to light and to accommodation There was no rigidity of the neck The tongue was dry and coated His tonsils had been removed His breath was foul His pharynx was markedly injected His lungs were normal except for a few hypostatic râles at the bases His heart was normal The abdomen was flat, the spleen and liver were not palpable All his deep tendon reflexes were present, there was no tremor of the hands

On admission his temperature was 104° F, pulse 96, and respirations 24 He ran a slightly irregularly continued fever for the next ten days when his temperature began to drop by rapid lysis, coming down to normal and remaining down thirteen days after his admission The entire febrile period from his initial chill occupied sixteen days During the course of the fever his pulse ran between 80 and 90

For the first three days after admission the eruption became

more marked, duskier red in hue, and more hemorrhagic in character During this time the headache was persistent, grew more severe, and the patient's toxemia became more profound At times there was marked delirium Six days after admission the eruption began to subside, the headache became less, and the toxemia was less marked The eruption and the headache had both practically disappeared by the time lysis set in As the fever began to drop, all evidences of toxemia cleared up and the patient rapidly improved With the disappearance of the fever convalescence set in and progressed rapidly His convalescence was unusually satisfactory considering the severity of the infection Three weeks after admission to the hospital, the patient could sit up and was discharged cured ten days later

Upon admission the leukocytes were 12,300, two days later they had risen to 23,500 The highest leukocyte count of 24,800 was reached five days after admission The polymorphonuclear neutrophils varied between 80 to 89 per cent The leukocytosis continued during the entire febrile period Twenty-four hours after the temperature had reached normal, the leukocytes were 13,000 Five days later they were normal—7500

Although high colored and scanty, his urine was normal throughout the course of the disease A Widal reaction for typhoid, as well as for paratyphoid A and B, was done four times, always with absolutely negative results A blood culture taken shortly after admission, was entirely negative The urine was cultured for typhoid bacilli, and on six separate occasions was found The stools were also cultured four times for typhoid fever bacilli, without any positive findings

The patient was admitted with the diagnosis of typhoid fever The complete absence of all bacteriologic evidence of this infection, taken in conjunction with the persistent leukocytosis, the clinical course of the disease, and the lack of all the characteristic signs of typhoid fever, forced us to abandon this diagnosis and to look upon the case as one of mild sporadic typhus fever or Brill's disease

It is unfortunate that the so called Weil Felix reaction was

not carried out during the active period of the disease   These observers[8] have shown that the blood of patients suffering with typhus fever agglutinates Bacillus proteus X 19 in the great majority of cases   The exact relationship of this reaction to typhus fever is not clear   Although the Bacillus proteus can in no way be regarded as the causative agent in typhus fever, this reaction is of decided diagnostic value   Had this reaction been carried out, our diagnosis could have been confirmed beyond reasonable doubt   As it was, it rested upon the complete absence of all evidences of typhoid fever and the clinical picture which corresponded closely to the accepted description of Brill's disease

The essential features of this mild form of typhus fever are as follows   The incubation period is short, lasting rarely more than five days   The onset is sudden, the disease is usually ushered in by a severe chill, sometimes also with vomiting   Immediately after the chill the temperature rises rapidly to 103° to 104° F   It reaches its height in two or three days, and continues with slight diurnal variations for twelve to sixteen days, ending abruptly by crisis or rapid lysis, the latter rarely occupies more than three days   Headache is one of the outstanding symptoms   It develops at the time of the chill, is unusually severe and persistent and often lasts until the crisis   Backache is also an early and troublesome symptom   Marked prostration and profound toxemia develop during the first day of the disease, become more marked during the first week, and frequently last until the fever begins to abate   The eyes are suffused and there is marked flushing of the face   Within forty-eight hours from the onset, the patient sometimes becomes delirious, but for the most part, is dull and apathetic   As a rule the pulse is slow in proportion to the height of the fever and dicrotism is not rare   The skin is hot and dry, and an eruption is a constant feature of the disease   The eruption may come out from the second to the sixth day   It first makes its appearance over the abdomen and back, and rapidly spreads to the arms and thighs, at times to the forearms, hands, legs, and feet   The rash comes out practically all at once and does not appear

in crops   It consists of a dusky red, slightly elevated macular eruption   As the disease progresses there is a decided tendency for the eruption to become petechial   It does not disappear on pressure   It persists practically throughout the course of the disease, disappearing rapidly about the time the fever drops There are few abdominal symptoms, pain and diarrhea are rare, constipation is the rule   With the defervescence of the fever, the symptoms rapidly disappear and convalescence is quickly established   Convalescence is usually uneventful and recurrences rarely occur. A polymorphonuclear leukocytosis is invariably present, the leukocyte count ranging from 11,000 to 24,000   In the majority of cases the spleen is palpable Complications are rare, bronchopneumonia being the most frequent   The prognosis of sporadic typhus is uniformly good, practically none of the patients die

The disease is most common between the twentieth and fortieth years of life   Males are more often attacked than females   The reported cases indicate that the disease is more prevalent among the Jewish population, but its occurrence is not limited to any nationality

A review of the symptoms of the case under discussion shows that the essential features of Brill's disease were present The onset was sudden and was accompanied by a chill, the fever rose rapidly, continued with some diurnal variations for about thirteen days, terminating by rapid lysis   Headache, backache, marked prostration, and a typical eruption were the outstanding features, and the blood constantly showed a leukocytosis

The disease with which the sporadic typhus fever is most apt to be confused, and from which it must be differentiated most often, is typhoid fever   In order to emphasize this differential diagnosis, it is helpful to compare these two infections

Typhoid fever		Typhus fever
14 days	Incubation period	4 to 5 days
Prolonged	Prodromata	Short
Gradual	Onset	Abrupt
Rare	Chill	Usually present

Typhoid fever		Typhus fever
Irregularly continuous from 3 to 6 weeks with diurnal variations, ending by a prolonged lysis	Fever	Continued fever for weeks, slight diur variation, usually e ing by crisis, or ly which occupies more than three da
Frontal, for the first week	Headache	Severe, prolong throughout the dise
Common	Epistaxis	Rare
Late	Prostration and toxemia	Early and marked
Not characteristic	Facies	Characteristic suffusi injection of the c junctivæ
Typical roseolæ disappear on pressure, come out in crops, develop during the second week of the disease	Eruption	Generalized, maculopa ular eruption D not disappear on pre ure, comes out sim taneously within couple of days of on and becomes petech
Common	Diarrhea	Rare
Frequent	Intestinal hemorrhages	Never
Persistent leukopenia	Blood	Definite leukocytosis
Blood culture positive early in the disease Widal positive Stools and urine contain typhoid bacilli	Bacteriologic findings	All the bacteriologic sig of typhoid absent, b a Weil-Felix reacti positive during the f brile period of the di ease
Common	Relapses	Rare
Prolonged	Convalescence	Rapid
Grave	Prognosis	'Uniformly good

If these distinctions are borne in mind there should be littl difficulty in differentiating these two diseases that have heretc fore been so frequently confused

In addition to typhoid fever there are several other condition from which Brill's disease, from time to time, may have to b differentiated In cases of typhus fever that show marke nervous manifestations, such as a transient Kernig's sign, activ delirium and excessive headache, the possibility of meningiti may have to be considered The different course of this latte

disease, together with the increasing signs of meningeal irritation, and the characteristic findings in the cerebrospinal fluid upon lumbar puncture, enable one to readily differentiate the two diseases

The diagnosis of Brill's disease from influenza may, under certain circumstances, present difficulties   The onset of influenza is frequently ushered in by a chill, the temperature rises rapidly, severe headache and marked prostration are not uncommon symptoms   On the other hand, in influenza marked involvement of the upper respiratory tract is common diarrhea is frequent, the pulse is, as a rule, rapid, the characteristic eruption of typhus fever is absent, leukopenia is the rule, and complications are common

Before concluding it should be noted that the mild sporadic form of typhus fever is little, if at all, transmissible   It is rare for more than a single case to occur in any one family   Although it is certain that the epidemic form of the disease is louse-borne, it is rare to find any evidence of louse transmission in the type of the disease here under discussion

The clinical picture of mild sporadic typhus fever seems to be so definite that if the possibility of its existence is not overlooked, its recognition should not be difficult   The clinical and bacteriologic studies of numerous observers, carried on over the past twenty years, show conclusively that a mild form of typhus fever is constantly present in most of the large cities of this country   It behooves us, therefore, to bear this in mind, and be more alert in the recognition of this disease

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CONTRIBUTION BY DR JOHN C GITTINGS

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PROPHYLAXIS IN CHILDHOOD[1]

IN looking over the pediatric literature of the 18th and 19th centuries, it is interesting to see the value which the relatively uninformed physicians of those days attached to measures for prevention of disease Today the physician who is not fully alive to these possibilities is in danger of sacrificing his high status in the estimation of his community

The present accepted and proved methods of prevention may be very briefly considered from the pediatric standpoint

Prenatal care and the avoidance of injury at birth belong to the province of the obstetrician Lues in the child would be largely preventable were it possible always to institute early and rigorous treatment of the mother The importance of the mother's diet for the child's intra uterine development, particularly in the antirachitic factors, is no longer debatable Careful analysis of the effect upon the child of the various stresses and strains of parturition is pointing the way to the avoidance of some of the serious birth injuries

It is unnecessary to consider the importance of cleanliness and asepsis in the avoidance of miscellaneous contagions, such as thrush, conjunctivitis, wound sepsis, etc Specific prevention is now beginning to bulk very largely in the practitioner's daily work

The value of toxin antitoxin in the prevention of diphtheria is one of the most securely established facts in preventive medicine and its use should be strongly urged for every child

[1] Read before the College of Physicians Philadelphia Pa. May 1 1929

From six to twelve months is the best age and in the late spri
or early fall the best time for its administration   If the histc
shows any evidence of asthma or stubborn eczema it is sa
to test for sensitivity before giving the first injection   Four
six months after the toxin-antitoxin injections have been give
a Schick test should be done to determine whether immun:
has been acquired   If not, a second course of injections will
almost uniformly successful   The Schick material must
freshly mixed and tested for potency   The only disadvanta
of toxin-antitoxin injections is that they may sensitize t
patients to horse serum

The status of prevention in scarlet fever is marred by t
fact that the injections often cause serious reactions and th
we are not yet certain that the protection will last more th
two or three years

The use of convalescent serum in the prophylaxis of meas]
is now on a well-established basis   If blood from a recent
convalescent patient is used, a dose of serum from 2 to 5 c
according to the age of the recipient, will prevent measles
95 per cent of cases, if given from three to five days after e
posure   Larger doses, 5 to 10 c c , may be used for those e
posed longer than five days   If measles is not entirely prevent
it will probably be more or less mitigated in 50 per cent   Wh
the donor is a healthy child, a Wassermann test is hard
essential

The difficulty of securing donors and of preparing the seru
suggested the use of whole blood from parents   Thirty c
of whole blood removed from a parent who has had meas]
and injected at once intramuscularly, has somewhat the san
effect as convalescent serum, although it is not a comple
preventive unless used early   Theoretically, it is safer to ha-
a preliminary Wassermann test done on the parent   A mi
attack of measles has the advantage of conferring active in
munity, whereas complete passive immunity induced by serum
short lived

In the same way immune serum may be used in the ca
of mumps and of varicella

Vaccine prophylactic therapy for pertussis is probably of some value if given early, but its results are by no means uniform or trustworthy

The administration of low virulence tubercle bacilli by mouth to newborn infants, as advocated by Calmette and Guerin in France, is not yet generally accepted as a safe procedure The theory is to effect a localized mild tuberculous implantation which will not progress to clinical disease, but which will stimulate resistance to virulent infection from human sources It was intended only for such infants as could not be removed from a definite tuberculous milieu Separation of the newborn child from all contact with open cases of tuberculosis still remains the most dependable means of preventing tuberculosis in early life

Of the prevention of typhoid fever or smallpox it is hardly necessary to speak The limitation of effectiveness of the typhoid prophylactic seems to have been reduced to three years at best There is reason to believe that a single injection yearly after three years will perpetuate protection

Recently there have appeared in literature, chiefly from abroad, a few instances of encephalitis which have followed smallpox vaccination Obviously this may prove to be a real calamity unless the cause is discovered and removed Apparently infants are much less susceptible than older children and adults and there is at present not the slightest reason to withhold vaccination of infants in this country

It is becoming customary to give tetanus antitoxin for every wound regardless of the circumstances Were the injections entirely innocuous, there would be less objection, but apparently reactions are more severe with this serum than with any of the others It should never be used without previous tests for sensitivity It would also seem desirable to limit its use to punctured or deep wounds, or those which cannot be promptly and thoroughly cleansed

The prevention of hydrophobia requires quick action If the circumstances show any suspicion of the biting animal's having been rabid, the prompt examination of its brain for

Negri bodies is essential   When this is not feasible the pre-
ventive inoculations should be given at once   ;

Marasmus used to be a common diagnosis and cause of
death   At autopsy most of these infants showed no lesions
sufficient to account for death   In some of these instances a
suppurative otitis and mastoiditis through the accompanying
toxemia may have been the cause   In most, however, the
fault lay in the feeding   Today, given reasonably intelligent
co-operation on the part of the mother, and an adequate eco-
nomic status, the vast majority of infants should escape maras-
mus   Next to the improvement in the milk supply, the most
important factors in this saving of life have been the deter-
mination of the child's caloric needs on the basis of his ex-
pected—not actual—weight, rational methods of preparing milk
for feeding, recognition of the importance of vitamins and of
the dangers of too heavy clothing and of poor ventilation

The use of citrous fruit juices or tomato juice in sufficient
quantity prevents scurvy   The juice of oranges which have
been kept in cold storage long after being picked is not as ef-
ficacious as that of the fresh crop and should be given in larger
doses

Rickets may be largely, but not absolutely prevented in
all patients by the use of potent cod-liver oil, begun at the end
of the third or fourth week of life   Sunbaths in summer and
ultraviolet light treatments once a week in winter, in conjunc-
tion with cod-liver oil, will almost entirely prevent rickets,
provided the general diet and hygiene are suitable   A few pa-
tients, particularly among negroes and Italians, may prove to
be partially resistant   The use of activated ergosterol prom-
ises to be even more effective than cod-liver oil in the prevention
of rickets   It is important to remember, however, that ergosterol
does not contain vitamin A, as does cod-liver oil

Spasmophilia and tetany—the chief causes of convulsions in
infancy—can be prevented by early and adequate use of anti-
rachitic measures

Tonsillitis and quinsy can be prevented by complete tonsil-
lectomy but sore throat, involving other lymphatic elements,

may still occur, although it is not as severe, as a rule, as true tonsillitis

Apparently some cases of spasmodic stenosis of the pylorus are accompanied by, if not caused by, hypertrophy of the thymus The syndrome of functional stenosis can, in such cases, be prevented by irradiation of the thymus

Celiac disease can probably be prevented if more attention is paid to the diet of children in their second year Since these children suffer primarily from starch indigestion, the habit of feeding large amounts of starch for supper as well as breakfast, and the free use of unstrained vegetables, is to be avoided in infants who evidence any tendency to intestinal indigestion

Certain individuals seem to be prone to develop the rheumatic syndrome The child who has a tendency to develop tonsillitis, myalgia, and growing pains, who tires easily and who may be somewhat anemic, requires careful supervision, especially in the late winter and spring All infected foci should be cleared up, the child should avoid chilling and physical exhaustion and should have occasional courses of salicylates alternating with iron and cod-liver oil Constipation should be avoided and the diet and daily regimen supervised In spite of this, rheumatism and heart disease will occur in some, but the incidence can be lessened by such measures Maude Abbott insists that patients with congenital heart disease require all these prophylactic measures, since an endocarditis engrafted on a congenital lesion is not unusual

Chorea is less amenable to preventive tonsillectomy than is rheumatism

The ascending route of infection in pyelitis is definitely to be accepted The avoidance of introducing infection into the vagina of infants, especially those with diarrhea, by careless ness in bathing probably has a practical importance In fection from toilet seats also is to be avoided

Nutritional anemia is the commonest form in infancy Persistence too long on a strictly milk diet and the lack of iron containing foods are the usual remediable causes

Tuberculous adenitis is due in large part to the use of raw

milk from heavily infected tuberculous cows Since the adoption of pasteurization of market milk in cities and the introduction of certified milk, tuberculous adenitis is becoming a clinical rarity

Simple goiter in early adolescence usually can be prevented by the exhibition of iodin Two grains of sodium iodid three times a day for a week, twice a year, seems to replenish the content of iodin in the thyroid gland

The infant who shows a tendency to exudative diathesis, by patches of moist dermatitis back of the ears and on the cheeks, often has a low tolerance for cow's milk fat Reduction of the amount of this fat in the diet and an increase of cod-liver oil to supply the deficiency of vitamin A will, at times, prevent a serious outbreak of eczema

Finally, several evenings could be spent on the most important questions related to child training

No one who has seen the results of a rational regimen, contrasted with those obtained by the over-solicitous or the behavioristic methods, can doubt that much of the individual's happiness and health, both in childhood and adult life, depends upon the parent's sense and knowledge, or lack of them

To see the spoiled, fretful, undernourished child transformed into the antithesis of these, within a few weeks, by separation from the family and introduction into a suitable regimen is a demonstration that can scarcely be misinterpreted

It is probably true that students and physicians, as a class, are not as interested in prevention as they are in cure The chief reason for this, it seems to me, is that the effects of preventive practices are not obvious The cure of diphtheria by antitoxin is a striking, tangible and satisfactory result On the other hand, the child who is given toxin-antitoxin may never have developed diphtheria and even a satisfactory Schick test gives negative results Only those physicians who study statistics can get a true idea of what prevention really means and he who is alert to the possibilities of prevention not only has the satisfaction of a clear conscience but also wins the real confidence and affection of the families that he treats

CLINIC OF DR WILLIAM EGBERT ROBERTSON

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THE ETIOLOGY AND PATHOLOGY OF ARTHRITIS

Nothing of a constructive nature is accomplished by the admission of ignorance, but truth impels one to admit his utter lack of knowledge of the cause of many cases of arthritis There are some who regard all forms of joint inflammation as infectious, resulting in mild or severe, acute, subacute or chronic varieties The similarity in end results between some of the known infectious forms and those not frankly infectious, would seem perhaps to justify this view To me, this speculative method is less attractive than a non committal attitude, unless evidence is incontrovertible Once committed in any degree to positivism, it is practically impossible to remain open-minded I prefer, therefore, to look upon arthritis in an etiologic sense, as being 1, Infectious, 2, metabolic, 3, unknown

Exception may be taken by some to the inclusion of acute rheumatic fever among the infectious group, because of the question as to the exact cause In recent years, evidence has been accumulating, both clinical and experimental, which is, to my mind, quite definite The Streptococcus hemolyticus or viridans can be recovered in a larger proportion of cases of rheumatic fever, than can the typhoid bacillus be cultured from cases of typhoid fever, yet no one questions the rôle played by the typhoid organism Clinically, no two cases of typhoid fever are quite alike, and rheumatic fever also presents clinical differences, especially when one includes the age factor In children, joint phenomena are apt to be evanescent or altogether overlooked, while the endocarditis I regard, with Sir Arthur Newsholme, as a constant In young adults the joint phenomena

are more marked and often intense, the endocarditis and other serous membrane involvement being less obtrusive and less destructive, except in recurrent cases, in which the original infection began in childhood   I prefer, therefore, to include rheumatic fever among the infectious types   Unlike some of the infectious variety, rheumatic fever does not cause destructive changes nor eventuate in deformity   It is essentially a periarthritis with more or less synovial effusion   Dr Small's work in this connection is of much importance   Not only has he succeeded in isolating a subvariety of the streptococcus group, the Streptococcus cardio-arthritidis, by cultural and serologic methods he has also found that many of the chronic, more or less deforming, types are apparently due to the same organism   If this is confirmed, it must cause us to change our opinion very materially   In the deforming group, endocarditis occurs so rarely as to justify the view, that when present, it is incidental, and not related, as cause to effect   In the frankly acute rheumatic fever cases, endocarditis may be regarded as virtually the dominant lesion, certainly the most destructive, while the joint lesion though often exquisitely painful, is totally recovered from

Some of the infectious types are deforming, as gonorrheal, or destructive, as the tuberculous, and the syphilitic also may be, as may septic and pneumococcic varieties   In general, the infectious forms are so definite and so readily understood as to causation and resulting joint pathology, that no further comment is necessary, with one exception

When in the course of, or more frequently some time after, an attack of typhoid fever, a joint becomes involved, it is most apt to be an expression of more or less widespread involvement of the marrow   In one case of this type multiple sinuses developed about the left knee-joint a few months after recovery from the original attack of typhoid fever   Regarding it as tuberculous, one surgeon refused to operate, advising rest and hygienic measures   Having recovered the typhoid organism from the sinuses, I elicited the help of the late Dr G G Davis, then Professor of Orthopedic Surgery at the University of Penn-

sylvania   The first operation was a failure   It was not radical
enough   At a later date he chiseled into the shaft of the femur
following a sinus for a distance of two-thirds the length of the
femur above the knee-joint   At the upper end we found three
tiny sequestra, removed them, cleaned out the lower two thirds
of the marrow cavity, and complete recovery followed with
return of function of the knee-joint   This was some years
ago   The patient has since been quite well but for a severe
type of hay fever each year

The metabolic forms are limited to those occurring in the
course of scurvy and those resulting from gout and those follow-
ing injections of sera   Perhaps some of the purpuric types
might be included, and those following the ingestion of such
drugs as iodids, quinin, lead or the salicylates, or after snake
bite, or following the use of bacterins or after transfusion   No
question will arise as to the justification for including scurvy
and gout as metabolic disorders   As to the other conditions
named, including Schönlein's and Henoch's purpura, we are
still in doubt as to the actual mechanism   When joint involve-
ment occurs in any of the purpuras, the joint lesion consists
of a more or less marked hemorrhagic extravasation in con-
nection with the periosteum and perichondrium, and some
degree of bone marrow involvement, especially hemorrhage
Some degree of synarthrosis may follow periarticular fibrous
change or even fibrosis within the joint

Scurvy is occasionally met with in artificially fed infants, in
the form of Moell Barlow or Barlow Cheadle disease, as it is
variously called   Here there is depression of bone marrow
function, marrow hemorrhage, and extravasation of blood be
neath the periosteum of the bones, both shaft and epiphyses
The same features occur in scurvy in adults, only in more
marked form   Fortunately rare today, severe lesions could
not persist for any length of time   Gout is apparently the
result of morbid, protein catabolism   The joint changes are
characterized by deposits of monosodium urate, needle-shaped
crystals, in the joint cartilages and other cartilages, in liga-
ments, tendons, and synovial membranes adjacent to joints

Tophi are masses of such crystal formation Marked deformity and disturbance of joint function may result In saturnine gout also, joint changes may be present, but as in some cases of true gout, the chief incidence may be upon the kidneys and blood-vessels

The third and last group, the group in which the cause is unknown, furnishes the greatest interest for us Comprising as it does the majority of cases presenting joint lesions of a deforming character, both because of its frequency and its destructive effects, it challenges our attention Arthritis deformans, or rheumatoid arthritis, is a disease as old as our knowledge of the human kind, though not confined to the human species alone It is met with at all ages, about twice as frequent in the female as among males, and in them more especially about the period of menopause The colored race is relatively seldom attacked

Deforming arthritis may rarely begin in an acute fashion As a rule it is insidious in onset, gradual and chronic in course, and more or less deforming The term "rheumatoid arthritis" is often applied to the less destructive cases, where the morbid anatomic change is chiefly in the synovial membranes and periarticular tissues

Osteo-arthritis, on the other hand, implies atrophy of the cartilage with productive bony changes in and about the articulating surfaces, or even bony overgrowth along the shaft of a long bone Indeed, various classifications have been made, based on some clinical or morbid anatomic state From the gross and microscopic pathologic standpoint, the view taken by Nicholls and Richardson makes for simplification They divide all cases into two groups first, proliferative, second, degenerative Whether these are the result of some infection or not is unknown Certain it is that the gonococcus may cause morbid changes quite like those of the rheumatoid type of Garrod The fact that no blood-stream infection has been found, and no growth results from joint cultures or from synovial fluid cultures, has cast doubt on their origin from micro-organismal infection

Rosenau, however, has had a large measure of success in culturing tissue in proximity to a joint, and lymph glands draining joints, after finely dividing the structures by means of sterile sand, and employing partial oxygen pressures much below the normal in culture tubes by means of stab cultures Focal infection as the prime event is not a recent concept It has been mentioned by various observers over a period of many years Goldthwaite and his coworkers, seem to have been divided as to the relative influence of infection and faulty posture, but they stated their belief quite clearly that focal infection is a matter of much importance Rosenau, then of Chicago, now with the Mayo's, and Billings of Chicago are largely responsible for the almost rabid manner in which focal infection has been seized upon as an etiologic factor Certain it is that a root abscess may suffice to invite severe and wide spread joint involvement This does not give license, however, for the wholesale extraction of teeth, which has become so common Devitalization should be sought for just as faith fully as root infection, and pyorrhea and gingivitis should be strenuously combated

It is not necessary to detail the sites of possible primary infection The removal of such a focus or even foci rarely leads to much, if any improvement Perhaps the time factor plays a part, but at least, the failure to improve casts some doubt on the infectious nature of the joint lesion Few would go so far as Sir Arbuthnot Lane in his condemnation of the colon Yet the participation of the colon by way of putrefaction or some other bacterial change of its content, cannot be lightly set aside Admitting it, however, does not lighten our task Closely allied to this is the question of diet, quantitative and qualitative Overeating often seems to be a factor in mid or late adult life It is a striking fact in adults at least that the initial appearance of a polyarthritis has often been preceded by some deep emotional strain or financial worry It seems to occur with sufficient frequency to make it more than coinci dental, but again even acceptance of the view does not lessen the seriousness of the situation, nor offer a definite solution

Based on analogy, I think the evidence favors the view that deforming arthritis is infectious, but we lack proof of a convincing nature, hence the advisability of placing it, at least etiologically, among the unknown In a large number of cases there are in fact, equally strong reasons for regarding this condition as due to some fault in metabolism Prolonged sugar elimination has been found in this disease, even proportional to the severity of the case

Proliferative arthritis deformans, perhaps better termed the atrophic type, may develop in the young or old Its onset may be acute, even resembling for a time articular rheumatism The many joints involved at one time, especially the smaller joints, the lameness and stiffness, and absence of endocardial or other serous membrane involvement, sooner or later make the differentiation Granulation tissue early covers the joint cartilage and the synovia gradually thicken Adhesion of opposing granulation layers leads to partial or complete obliteration of the joint Fibrous or even bony ankylosis may result Rarely the marrow cavities of adjacent bones may become continuous The bone is often rather soft, rarefaction occurs, but exostoses do not develop Bone and cartilage may become stratified, eventuating in dense, fibrous ankylosis The joints enlarge, but do not present irregularities or nodulations When the disease involves the spine, the various articulating surfaces of the spine and the costovertebral articulations are attacked, resulting in more or less rigidity of the spine In the Marie-Strümpell type, the hips and shoulder joints are also involved The von Bechterew type involves part or even the entire spine This latter is very common in the lower portion of the spine, often simulating sacro-iliac disease and sciatica, and may give rise to various reflex phenomena Still's disease is a variety of the proliferative form, occurring in children, most often in girls, associated with some enlargement of the spleen and lymphadenopathy

Degenerative Arthritis Deformans —This is met with most commonly in elderly people and, as a rule, fewer joints are involved, but the deformity may be very marked It varies

from the slowly progressive and relatively innocent deformity of the phalanges, known as Heberden's nodes, to the most marked and irregular nodular deformity of small and large joints   Insidious in onset, its course is afebrile and slowly progressive   Granulation tissue is absent in this type, the cartilages being first involved, then the bone   Softening and disintegration of cartilage take place, bone often opposing bone, hence becoming smooth and eburnated   Around the margins of the joints bony and cartilaginous nodulations develop   Joint mice, due to contracted cartilage, may exist

There is, as a rule, very marked rarefaction of the bone except in the immediate vicinity of the opposing bony surfaces   True ankylosis does not occur in this variety, but the subluxation, eburnation, nodosities about the joint, all tend to fix it more or less, and to cause very great deformity in many cases

CLINIC OF DR JAMES E TALLEY
Assisted by DR H R GLENN

INCIPIENT LIPOID NEPHROSIS AND PHENOL-PHTHALEIN POISONING

THE various preparations of phenolphthalein meant for laxative purposes are so much like candy that it is easy for children, as well as adults, to cultivate the habit of using them too freely That the drug may not be as innocuous as is usually supposed is suggested by the history of the patient we wish to report, who was admitted to the Presbyterian Hospital four times from July, 1927 to March, 1929

She is a young, unmarried woman, twenty-one years old 5 feet in height and weighs 112 pounds In 1924 she weighed 180 pounds, and her picture at that time showed that she was very obese looking Under diet she reduced herself to 110 pounds

In July 1927—her first admission—she said she had been in ill health for two years Her chief complaints were nervousness weakness, vertigo, insomnia, generalized pains, palpitation, some dyspnea, and she was markedly pale She craved sweets, indulged on occasions, and afterward had attacks of nausea and vomiting She was markedly constipated for which she had been taking, since March 1926, a well known phenolphthalein tablet which contained 1 3 grains She had been gradually raising the dose until now she takes from 32 to 48 tablets at a time Evidently she did not stress the edema at this time, but notes taken from her diary show that it had already begun to appear Her heart was normal in size and function, her blood pressure 118/80, and the blood count was

Hb 78 per cent , R B C , 3,900,000, and W B C , 7300   The differential count showed a slight increase of the lymphocytes with a corresponding decrease in the polymorphonuclears   Micturition was frequent and in small amounts, but the average output at this time was from 40 to 50 ounces per day   The average specific gravity was from 1 025–1 030, the menses were scant, the stools, the sputum, and the fractional test meal were all normal   She was looked upon as a patient with mild anemia and slight psychic depression   Although her blood count was not low, her pallor seemed very marked   On rest, iron and arsenic injections and the Minot-Murphy diet, she made great improvement and gained in weight   She was readmitted in October, 1927   She had been better for a time but gradually felt herself growing worse again   There was the same color, apathy, and weakness and the same perverted appetite for sweets, in which she indulged and following which she drank much water   Although she claimed that her face, ankles, and hands swell at times, there was no actual edema noted at the time   In this patient, the tightness of her rings and decreased mobility of her face preceded any demonstrable edema of the ankles, especially when in bed

The constipation was still extreme and she was using on an average of 37 tablets a day frequently when she took them   Each tablet contained 1 3 grains of yellow phenolphthalein   Her eye-grounds were normal   The urine showed an average specific gravity of 1 007   There was a faint trace of albumin, no sugar, and, microscopically, a few leukocytes   The stools were normal, her blood count was Hb 75 per cent , R B C , 3,960,-000, W B C , 7000, and the differential showed 60 per cent of polymorphonuclears, and 36 per cent of lymphocytes   Her blood sugar was 109 mg per 100 c c of blood   The basal metabolism was —26 per cent   She was again treated as an anemic with hypothyroidism, encouraged as a psychic, and she showed marked improvement   At this time she had small doses of desiccated thyroid gland   On January 26, 1928 the patient was again readmitted with practically the same symptoms, but this time with swelling of the entire body, constipa-

tion was a dominant element   For two months she had been taking larger and larger amounts of the yellow phenolphthalein tablets   One night recently she took 64 tablets, which means over 83 grains of phenolphthalein   During that night she had pain in the precordium, and fainted   As her cardiovascular apparatus was normal, it is probable that the pain arose below the diaphragm   She still had the same love for sweets, and drank large quantities of water after eating them   This caused general anasarca, including some ascites, but she had found that this large number of phenolphthalein tablets produced a great number of liquid stools which relieved the edema   Her temperature, pulse, and respiration were normal, blood pressure was 130/90 on admission   Disturbed by the edema she now voluntarily cut down the intake of liquid, which she was allowed to do to see the result   The average intake was now about 16 ounces and the output about the same   The urine had an average specific gravity of 1 020, it was acid, there was always a trace of albumin, but no sugar and, microscopically, there were now some hyaline and light granular casts, as well as a few leukocytes   The blood urea nitrogen was 12 mg and the blood sugar 96 mg per 100 c.c of blood. The Wassermann was negative The blood count of admission showed Hb 61 per cent , R B C , 3,210,000, and W B C , 6950, with a differential of polymorphonuclears 60 per cent and lymphocytes 35 per cent When she left the hospital about three months later, the Hb was 79 per cent , the R B C were 3,890,000 and the white corpuscles 6350

Her pelvic examination was negative   The x ray showed a large, flabby, non functioning gall bladder   Gastro intestinal x ray showed simply gastric ptosis   The stools were always normal   The sella turcica was x rayed and found to be normal Before she left the hospital the casts had entirely disappeared from the urine, but a trace of albumin remained   During this admission she was at times depressed, but was cheerful when she left the hospital in March, 1928   The same month she developed a small fissure in ano for which she was admitted for operation   During this time the urine was acid, specific gravity

1 025, trace of albumin, no sugar, and, microscopically, it was negative

The last admission was in February, 1929, because of general anasarca She was seen on February 14, 1929, when her weight was 125 pounds   Two days later it had increased to $141\frac{1}{2}$ pounds, as she predicted it would if she omitted the phenolphthalein tablets

By this time she had found that in order to get rid of this general anasarca, which included the face, body, legs, hands, and some ascites but no effusion of the pleural cavity it takes 2 to 3 doses on succeeding nights of from 64 to 80 phenolphthalein tablets at each dose   This provokes marked purging so that she may go to bed weighing 125 pounds and in the morning find it reduced to 116

She reports she had been fairly well for a time after leaving the hospital, had the same desire for sweets and bitter and sour foods, the constipation had been marked throughout and although the phenolphthalein tablets in such large doses made her weak, she knew of no other laxative that would reduce the swelling   After indulgence in sweets, according to her story she has taken as many as twenty glasses of water a day in addition to milk   Her average weight is now 113–116 pounds   This time the urine was found to acid, specific gravity 1020, albumin, a trace or none, sugar, none   There were no casts, but a few leukocytes   The phenolsulphonephthalein test, taken when the anasarca was better, showed a total of only 40 per cent   The Mosenthal test showed a variation of ten points   The basal metabolism was −19 per cent   The R B C were 4,000,000. W B C , 10,000, and Hb 82 per cent   The polymorphonuclears were 57 per cent , the lymphocytes 38 per cent , the transitionals 3 per cent , and the eosinophils 2 per cent   The blood-films appeared normal   The blood sugar was 114 mg per 100 c c of blood, and the blood urea nitrogen 22 mg   Three examinations of blood cholesterol at ten-day intervals gave 309 mg , 385 mg , and 455 mg per 100 c c of blood   The serum albumin was 5 1 per cent and the serum globulin was 2 5 per cent   At this time the blood-pressure averaged 100/70

In the beginning the patient had been looked upon largely as one of mild anemia, hypothyroidism, and psychic depression, with perhaps elements in her home surroundings which could not be rectified. With the advent of the anasarca and casts in the urine, on her third admission, one was more impressed with the evidence of an organic background and the partial parallelism between the patient's condition and lipoid nephrosis, suggestive though not conclusive, began to concern us. There was no history of pregnancy, diffuse glomerular nephritis, amyloid disease, tuberculosis, syphilis, or chronic suppuration. All of these are sometimes precursors of lipoid nephrosis. Since some look upon lipoid nephrosis as having its origin in disturbed metabolism it is possible that phenolphthalein might have a double effect, directly on the kidney interfering with water elimination and also through disturbance of metabolism. Lipoid nephrosis is characterized by insidious onset, chronic course, anorexia, fatigue, pallor, and at first, edema of the ankles, which may extend to the face the body, and the serous cavities. The urine is often small in amount and of high specific gravity, albuminuria is much more marked than in this patient, often with hyaline and granular casts, possibly from the diffuse glomerular nephritis which sometimes precedes. The urine also contains lymphocytes and epithelial cells, some of which may contain the double refractive lipoid cells, or they may exist as free granules in the urine. The blood count may be but little disturbed. On account of the albuminuria, when marked, the serum albumin is markedly decreased and the serum globulin is relatively and quantitatively increased. Cholesterol in lipoid nephrosis is markedly increased. In this patient, instead of the normal 140–170 mg per 100 c c, as given by Myers, we have 309 mg, 385 mg, and 455 mg per 100 c c. The blood urea nitrogen was practically normal and the phenolsulphonephthalein is somewhat reduced. In lipoid nephrosis the basal metabolism is as low as −20 per cent, this patient averages −24 per cent. In lipoid nephrosis there is no enlargement of the heart and the blood pressure is normal, just as it was in this case. By some oversight the double refractive lipoid bodies were not looked for until

the last admission, when there were none found   At this time there was no albuminuria and no casts   That there should not have been a greater lessening of the serum albumin and a corresponding increase in the serum globulin is explained in this patient by the fact that there was no constant loss of albumin in the urine such as there is in the average well-developed case of lipoid nephrosis

The relationship of the phenolphthalein tablets and the anasarca is interesting   In March, 1926, she was taking 3 or 4 at a time, by July, 1927 she took 32 to 48 at a time, in January, 1928 as many as 64 at a dose, and in February, 1929, as many as 80 a dose   That is, when she came under observation this last time she was taking as much as 104 grams of yellow phenolphthalein in one night   At first it was used to combat constipation, later, it was used to get rid of the anasarca which followed the eating of sweets and the drinking of large quantities of water subsequent to that   That there is a relationship between the ingestion of carbohydrate in the form of sweets with a sparsity of protein and the retention of water is evidenced by the fact that as soon as she was given a high protein diet, this retention entirely disappeared

With respect to the edema she first noticed it in 1926, nine months after beginning the phenolphthalein tablet   In February, 1927, her diary showed that she went from 117 to 134 pounds in three days   In February, 1929, we personally saw her go from a weight of 125 to 141 pounds in forty-eight hours   On January 13, 1929 in the morning she weighed 118 pounds and in the evening 123 pounds, that night she took 48 phenolphthalein tablets, and on January 16th she weighed 108 pounds   Again, on January 31, 1929 her weight was 137 pounds, she took 68 phenolphthalein tablets and on February 1st, it had fallen to 120 pounds   Thus the record runs until February 16, 1929, weighing $141\frac{1}{2}$ pounds she took 80 phenolphthalein tablets at night and the following day her weight was, in the morning, 127 pounds, and in the evening $121\frac{1}{2}$ pounds

There is but little written about the toxicity or even the physiologic effect of phenolphthalein, but we are able to glean

the following It is a crystalized coal tar derivative, dihydroxyphthalophenone, commonly used as an indicator, but also used for laxative purposes in doses of 1 to 7 grains

Concerning its physiologic action in therapeutic doses and its poisonous properties, if any, little sound experimental evidence is at hand Bastedo states that phenol is not liberated from phthalein after administration and that its laxative action is mild, non griping, and depends upon stimulation of peristalsis and, to some extent, on the prevention of absorption from the large bowel

Cushny states that some of the phenolphthalein is reabsorbed into the blood from the large intestine, carried to the liver, and returned to the intestine by way of the bile, so that it acts for several days as a mild laxative, gradually being eliminated in the stools and to a less extent in the urine As to its toxic properties, Wood has shown in experiments on dogs that doses which, in the human being would be equivalent to 60 to 100 grains, are quite harmless Abel and Rowntree give animals enormous doses intravenously without ill effects Orland reported a case in which a three-year-old child took 30 grains by mouth without showing any toxic symptoms On the other hand, Hydrick reported albuminuria following the ingestion of 1 to 2 grains in twenty consecutive tests, but Bastedo has not found a single instance of albuminuria following phenolphthalein in the course of frequent urine examinations during an extensive clinical use of the drug Thus it would seem that most experimental workers and physicians regard phenolphthalein as a laxative entirely lacking in toxic properties This statement is largely true in a large majority of cases, but there is no doubt that individuals have idiosyncrasies toward the drug Skin lesions, due to the ingestion of phenolphthalein over a long or short period of time, are a matter of common knowledge

This patient, then, showed many of the symptoms and signs of incipient lipoid nephrosis, as perverted and often lost appetite, fatigue, pallor, edema, and reduced urine In this particular case there was but mild albuminuria, so that there was but little disturbance between the serum albumin and serum globulin,

but there was a much increased cholesterol and lowered basal metabolism   The normal blood-urea nitrogen, the normal blood-pressure, and the normal heart are also worth noting   That the taking of such large quantities of phenolphthalein must have a profound effect on metabolism is shown by the remarkable water retention and the greatly increased values in cholester-inemia   The eating of candy freely is a common practice, but it leads to no such edema as this girl exhibited   Though she drank more water than usual after these indulgences, there was a decrease in water excretion with no other element to cause than phenolphthalein

This paper is written four months after the patient left the hospital, but she is seen occasionally   She has taken no phenol-phthalein since the last admission to the hospital, but is loath to indulge in sweets as that means thirst and the taking of more water and she has found the tendency to water retention still exists   The interference with this function of the kidney, originating, as far as we know, in the indulgence in large amounts of phenolphthalein, is still present

BRONCHIAL OBSTRUCTION

CAREFUL physical and roentgen ray examinations of the chest aided by bronchoscopy have revealed the not infrequent occurrence of bronchial obstruction in various intrathoracic lesions involving directly or indirectly the bronchi Bronchoscopy, or the direct visualization of the lower air passages, is the only method by which, in the majority of cases, an accurate diagnosis of the cause of bronchial obstruction can be made This is notably true in primary new growth of the bronchus and when narrowing of the bronchial lumen is the result of inflammatory changes, e g swelling of the mucosa the presence of thick tenacious secretions or of exuberant granulation tissue, or cicatricial contraction The important rôle which bronchial obstruction plays in the symptomatology and diagnosis of aspirated foreign bodies is now well known Much less common and impossible of recognition clinically without bronchoscopy are the rare congenital obstructions such as the one observed by Dr Chevalier Jackson in which a "congenital web" was present, the removal of which was followed by recovery The *extrabronchial* causes of bronchial obstruction are numerous, e g , the presence of enlarged lymph nodes, Hodgkin's disease, mediastinal new growths, aneurysm, new growths in the lung, enlargement of the heart, especially the left auricle, large pericardial effusion, etc.

The *results* of bronchial obstruction depend upon (1) The suddenness and the extent to which the entrance and exit of air to the corresponding lung is impeded, (2) the interference with the drainage of secretions from the same area, and (3) the presence or absence of infection

With *complete bronchial occlusion* the corresponding part of the lung collapses (obstructive atelectasis) as a result of absorption of the retained air   With *incomplete obstruction,* the exit of air on expiration is more impeded than the entrance of air on inspiration, with the result that the corresponding part of the lung becomes overdistended (obstructive emphysema)   In the presence of infection, an inflammatory reaction occurs which in the bronchi beyond the obstruction and in the corresponding lung area gives rise to exudates which cannot gain exit and eventuate in suppuration   The "drowned lung" in patients with aspirated foreign bodies and the pulmonary abscess secondary to primary cancer of the bronchus are significant in this connection   When obstruction is *partial* and more *gradual* in development (chronic obstruction) the bronchi distal to the stenosis gradually become dilated (obstructive bronchiectasis)

The clinical features and some of the problems involved in the diagnosis and treatment of patients presenting evidences of bronchial obstruction are exemplified in the following patients who have attended the clinic

Case I   Bronchial Obstruction with Obstructive Emphysema, Foreign Body Case —A child, aged one and a half years, suddenly had a severe paroxysm of choking and coughing, it had previously been observed playing with a piece of celluloid Wheezing respiration was noticed immediately after the attack On the basis of this, a diagnosis of asthma was made and the patient was given a number of hypodermic injections of epinephrin, the wheeze persisted and later, cough developed A roentgen-ray examination of the chest, made about three months after the accident, revealed a collapse of the left lung and some displacement of the heart   No particular significance was attached to this and treatment was continued on the basis of the condition being asthma with bronchitis   About eight months after the accident another physician was consulted, he found, on physical examination, that there was quite marked obstruction in the left bronchus   On close questioning he elicited the history of choking after playing with a piece of celluloid, a

INSPIRATION

EXPIRATION

Fig. 158 — Roentgenograms made at the end of inspiration and expiration in the case of a child aged one and a half years who eight mont ɪspirated a piece of celluloid At the end of *inspiration* the chest presents practically a normal appearance at the end of *expiration* th displaced to the right the left diaphragm is depressed and the left lung appears to contain more air than the right These pl from partial obstruction to the left bronchus air is allowed to enter the left lung but during expiration it is trapped producing o

tentative diagnosis of bronchial foreign body was made The patient was sent to the clinic for study When admitted, there was moderate fever A definite wheeze was heard at the end of expiration Physical examination disclosed definite evidence of interference with air entering and leaving the left lung A roentgen-ray examination of the chest revealed a marked obstructive emphysema involving the left lung (Fig 158) Bronchoscopy was definitely indicated on the history, the physical signs and the roentgen-ray findings, in fact it was indicated on the basis of any one of these At bronchoscopy there was found a piece of celluloid in the left bronchus There was very marked inflammation of the bronchial mucosa, a small quantity of pus was found The foreign body was removed without anesthesia, general or local The patient made a satisfactory recovery following the removal of the foreign body and the physical signs cleared promptly

Case II Bronchial Obstruction with Pulmonary Collapse and Drowned Lung, Foreign Body Case —A child, aged eleven months, was brought to the clinic with the history that for the past three weeks it had fever with cough and wheezing respiration There was a history that while playing on the floor, the child suddenly had a severe attack of choking and gagging A diagnosis of pneumonia was made and appropriate treatment was instituted The patient's condition did not improve, on the contrary it became progressively worse A roentgen-ray study indicated the presence of a rather extensive process involving the entire left lung and displacement of the heart to the left suggesting a partial pulmonary collapse A tentative diagnosis of non-opaque foreign body in the bronchus was made and the patient referred to the clinic The child was very ill, there were frequent paroxysms of coughing, the temperature was 102° F Physical examination revealed a very extensive lesion involving the entire left lung, there was marked impairment on percussion and on auscultation the breath sounds were very distant An occasional râle was heard Over the right lung the breath sounds were very harsh and many moist râles could

be heard The impressions gained by physical examination suggested partial obstruction of the left main bronchus with retention of a large quantity of secretion distal to this A roentgen ray study of the chest indicated the presence of a partial collapse of the left lung which was uniformly dense suggesting drowned lung There was also some displacement of the heart to the left Bronchoscopy was clearly indicated and was performed A large timothy head was removed from the left main bronchus The changes observed in the left lung following removal of the foreign body were not pronounced, it required several weeks before the signs of bronchial obstruction cleared This case is a sharp contrast to Case I where a foreign body remained in the bronchus for eight months and produced very little reaction with some obstruction to the air current but no obstruction to drainage The timothy head may have produced a temporary obstructive emphysema, but, because of its shape and the marked inflammatory reaction which promptly occurred, the airway was soon closed off

Case III Bronchial Obstruction with Collapse, New Growth —A man, aged thirty nine years, had been troubled with severe cough and some wheezing over a period of about eight months Recently he had some difficulty with breathing and was unable to lie on the right side The paroxysms of coughing were very severe, there was no expectoration and at no time had there been hemoptysis The physical signs indicated obstruction of the right bronchus with collapse of the upper portion of the right lung There was displacement of the heart to the right A roentgen ray study was made, this corroborated the findings of the physical examination (Fig 159) Bronchoscopy was clearly indicated There was found a fungating neoplasm which completely occluded the orifice of the upper lobe bronchus and partially blocked off the stem bronchus A specimen was removed for biopsy The histologic study showed carcinoma Deep roentgen ray therapy was recommended

Fig 159 —Roentgenogram of the chest of a man, aged thirty-nine years, who for eight months has had cough and wheezing respiration There is a complete collapse of the entire right upper lobe, and possibly the middle lobe The right diaphragm is very high and the heart is drawn towards the right side There is obstruction of the right upper lobe bronchus, possibly also the middle lobe bronchus There is nothing to indicate its character, it is very probably either foreign body, an endobronchial neoplasm or a compression stenosis The left lung shows a compensatory emphysema (Roentgen-ray report by Dr W F Manges)

Case IV   Bronchial Obstruction with Massive Collapse in Pulmonary Tuberculosis —A male, aged forty-five years, had been well until three years ago, when following an acute illness diagnosed as "grippe" he continued to cough and expectorate a mucopurulent sputum   Shortly afterward he was told that he had pulmonary tuberculosis with tubercle bacilli in the sputum He discontinued working for nearly two years, but during the past six months had returned to a light occupation   Recently he noticed an increasing shortness of breath, especially on exertion,

which he suggested might be due to his heart which two months previously had suddenly "started to beat on the right side" The physical examination revealed fair general nutrition, temperature 99° F and pulse 80 The trachea was displaced to the right side The right chest was flattened and immobile. The cardiac impulse was palpable in the fourth and fifth interspaces to the right of the sternum The percussion note throughout the right side was dull, and throughout the left side including the precordium, was hyperresonant The breath sounds over the dull area were blowing in quality and numerous coarse râles were audible There were no signs of cavitation The signs at first suggested extensive pulmonary fibrosis with contraction displacement of the trachea and heart The patient insisted that the heart displacement had occurred suddenly two months previously The roentgen ray study one year previously and just before admission showed striking differences The possibility of bronchial obstruction and pulmonary collapse suggested a diagnostic bronchoscopy which revealed a deviation of the trachea with compression stenosis of right bronchus apparently due to an extrabronchial lesion Sanatorium treatment was advised

Case V Bronchial Obstruction of Undetermined Etiology — A man, aged thirty-one years, had been perfectly well until four months ago when he was injured in an automobile accident There was a fracture of the left humerus and of the first rib on the right side He stated that at that time he had a collapse of the right lung Since the injury there has been some difficulty with breathing notably on exertion There is no cough or expectoration His weight has remained practically normal There has been no fever When examined at the clinic the left chest was found flattened and there was practically no movement with respiration The trachea was displaced to the left side The apex impulse of the heart was visible in the fourth left interspace in the anterior axillary line There was dulness

A   B
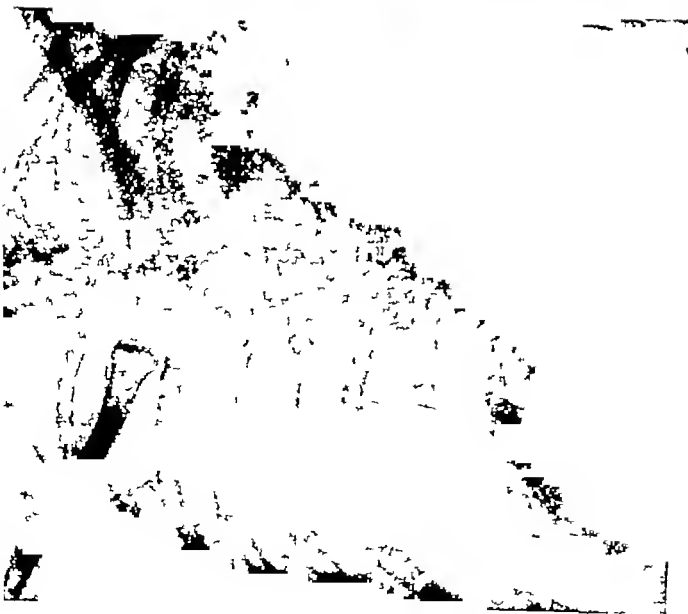
Fig 160 —Roentgenograms of the chest of a man, aged thirty one years, who developed a pulmonary collapse some time after being injured in an accident

A, This study made on admission shows a complete collapse of the left lung The trachea and heart are drawn to the left side, the right lung extends well beyond the left border of the sternum There is nothing to indicate the cause of the collapse

B, Roentgenogram made following the bronchoscopic instillation of iodized oil into the left bronchus The left bronchus which is dilated, terminates abruptly at a point about 3 cm beyond the bifurcation of the trachea The end of the dilated bronchus seems smooth No communication can be observed with the peripheral portion of the left lung (Roentgen-ray report by Dr John T Farrell, Jr)

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chest were distant All the signs pointed to collapse of the
eft lung, this was corroborated by roentgen ray study No
definite cause could be ascribed to this and bronchoscopy was
advised There was found displacement of the entire tracheo
bronchial tree to the left side The left main bronchus, which
was greatly dilated, terminated in a blind pouch about 3 cm
beyond the carina No communication with the distal portion
of the left bronchus could be found Iodized oil was instilled
and stereoroentgenograms made (Fig 160) These corroborated
the findings at bronchoscopy The bronchoscopic findings in
this case were extremely unusual and at this time no entirely
satisfactory explanation can be given The patient continues
under observation in the clinic In order to relieve the dyspnea
which was apparently due to extreme shifting of the mediastinum
to the left and overdistention of the right lung, an artificial
pneumothorax was done on the side of the collapsed lung This
was followed by marked relief of the dyspnea As stated the
patient continues under observation in the clinic and his progress
will be reported later

Case VI Bronchial Obstruction with Bronchiectasis —A
woman, aged twenty six years, had been troubled with frequent
cough and expectoration of a large quantity of pus since a severe
attack of pneumonia contracted fourteen years ago At times
the pus was fetid and occasionally it was blood streaked There
were irregular periods of fever Since the onset, there have
occurred four severe and acute illnesses, which were charac
terized by high fever, rapid pulse and respiration, marked weak
ness and cough which had suddenly become non productive
These attacks were diagnosed as pneumonia It is very probable
that they were due to bronchial obstruction with retention of
pus When free expectoration of pus recurred, the symptoms
subsided. In the intervals between attacks, constitutional
symptoms were absent and the patient led a normal life except
that there was productive cough with fetor The patient's
general physical condition was good Breath was fetid There
was very marked clubbing of the fingers Expansion was

definitely less over the left chest especially over the lower half Over this area there was dulness on percussion and breath sounds were suppressed   Scattered medium and fine râles were heard The diagnosis from the history, the symptoms and the signs was extensive lung suppuration involving the entire left lower lobe   Roentgen-ray studies made at this time showed a very dense shadow over the lower half of the left chest, in addition there were present areas which suggested cavities   The impression was that the condition was a marked bronchiectasis with considerable fibrous tissue formation   Bronchoscopy was recommended   Bronchoscopic findings were those of extensive lung suppuration involving the left lower lobe, in addition there was found a cicatricial stricture at a point 1 cm distal to the orifice of the left upper lobe bronchus   Pneumonographic studies were made which corroborated the diagnosis of bronchiectasis   Bronchoscopic aspiration of the pus with dilatation of the stricture was recommended

Case VII   Bronchial Obstruction Due to Compression of Bronchus —A woman, aged thirty-seven years, had been troubled with cough and dyspnea for about two years, the cough was non-productive, there was no history of hemoptysis   There was a slight loss of weight   The patient's general physical condition was good   There was no fever and at the time of examination there was no dyspnea   The expansion of the chest was limited on the right side   There was some dulness on percussion over the right back from the third to the sixth ribs Breath sounds were harsh over the right chest, and on coughing numerous medium and coarse râles and squeaks were heard over the right lung   The physical signs were rather indefinite but suggested a pathologic process involving the root area of the right lung   A roentgen-ray study revealed many rounded, sharply defined masses springing from the root of the lungs on both sides, more on the right   These suggested lymph-node tumors   Bronchoscopy was advised to determine if there was any endobronchial neoplasm and also to learn the condition of the bronchial tree   There was found a marked compression

stenosis of the right stem bronchus The bronchus in this
locality was fixed and the endoscopic appearance suggested a
peribronchial infiltrating lesion A diagnosis of compression
stenosis of the bronchus secondary to malignancy was made
Deep roentgen ray therapy was recommended

**Case VIII Bronchial Obstruction Due to Inflammatory
Changes and Secretion** —A man, aged fifty years, who had been
well until one and a half years ago developed a cough and dif
ficulty in breathing This apparently followed an acute
respiratory infection He was able to continue his work as a
machinist but was greatly distressed by frequent paroxysms of
coughing which left him exhausted and short of breath A
diagnosis of bronchitis had been made and treatment was pre
scribed but there was no improvement in the symptoms, which
instead became more severe, especially was this noticeable at
night The attacks also became more prolonged, at times
lasting for one week The patient noticed that the symptoms
were somewhat relieved if he had free expectoration, this did
not often occur during a paroxysm The sputum was pearly
gray, tenacious and lumpy He finally had a very severe paroxy
ysm and being unable to continue with his work he came to the
hospital for treatment He was extremely dyspneic, this ap
peared to be expiratory as well as inspiratory Epinephrine
gave temporary relief, all other medication seemed to have no
effect On physical examination the chest was found symmet-
rical, it was emphysematous in type and there was little move-
ment on respiration The percussion note was generally hyper-
resonant, the breath sounds were very feeble especially over
the lower lobes and many coarse and fine râles were heard
A roentgen ray study of the chest failed to reveal any localized
pathologic areas There was a general increase in the pulmonary
markings which suggested an inflammatory origin The nasal
accessory sinuses were examined and found to be practically
negative there was no demonstrable focus of infection in the
throat The question of allergy was investigated but no posi-
tive cutaneous reactions were obtained Bronchoscopy was

recommended   The mucosa of the trachea and bronchi was found thickened, inflamed, and granular, a large quantity of mucoid secretion was present in the right lower-lobe bronchus, a similar quantity in the left lower-lobe bronchus   Secretion was aspirated   There was a tendency for the bronchi to collapse during cough and expectoration   Following the bronchoscopy the patient was greatly relieved, breath sounds were heard more clearly over the lower lobes, few râles were heard   Bronchoscopic treatment was continued at regular intervals and the patient has been practically free from symptoms   This case represents one of the types of asthma where no definite etiologic factor can be found and no relief is obtained following the use of epinephrine   The physical signs indicated a definite tracheobronchial infection with, at times, temporary bronchial obstruction, this is the type of case that is usually benefited by bronchoscopic treatment

SUMMARY

The foregoing cases of obstruction to a bronchus were recognized as such by physical examination combined with roentgen-ray examination, it was impossible, however, to determine the cause of the bronchial obstruction   For this bronchoscopy was necessary and furthermore it was necessary to determine the cause of the obstruction before appropriate treatment could be recommended

CLINIC OF DR WILLIAM D STROUD

CHILDREN'S HEART HOSPITAL

THE TREATMENT OF RHEUMATIC CARDIOVASCULAR DISEASE IN CHILDREN

MUCH is being written concerning the treatment of rheumatic fever and its accompanying and resultant cardiovascular damage. The attitude of the average physician toward the results of such treatment is one of hopeless discouragement. Hence the unwarrantedly enthusiastic reception from time to time of apparently somewhat premature announcements of the discovery of organisms thought to be the etiologic factor in rheumatic fever

At present there seem to be three forms of treatment recognized as definitely established procedures or as having possible beneficial results

1 Rest, with salicylates in the acute arthritic (exudative) and pancarditic (proliferative) stage, followed by prolonged rest with nourishing food, fresh air, and sunshine in the subacute or more or less latent stage

2 Rest with antistreptococcus serum in the acute stage followed by prolonged rest, nourishing food, fresh air, sunshine, and vaccines in the subacute stage [1]

3 "Intravenous desensitization or immunization with suitable antigenic substances—building up the immunity so that the liability to renewed infection will be lessened, or, if new infection occurs, the reactivity of the tissue will approximate that of immunity without hypersensitiveness "[2]

An analysis of the results obtained at the Children's Heart Hospital in Philadelphia where for the past five years the type

of treatment has been confined entirely to that described as No 1, is reviewed in the following pages   Such a report has seemed to be of value for a number of reasons, among which should be included the attempt to establish an approximate base-line upon which we may perhaps be able to evaluate other types of therapy in the future   It may also serve to emphasize some of the many variables which are inherent in the problem   Perhaps the greatest of these variables, namely, the question of the permanency of
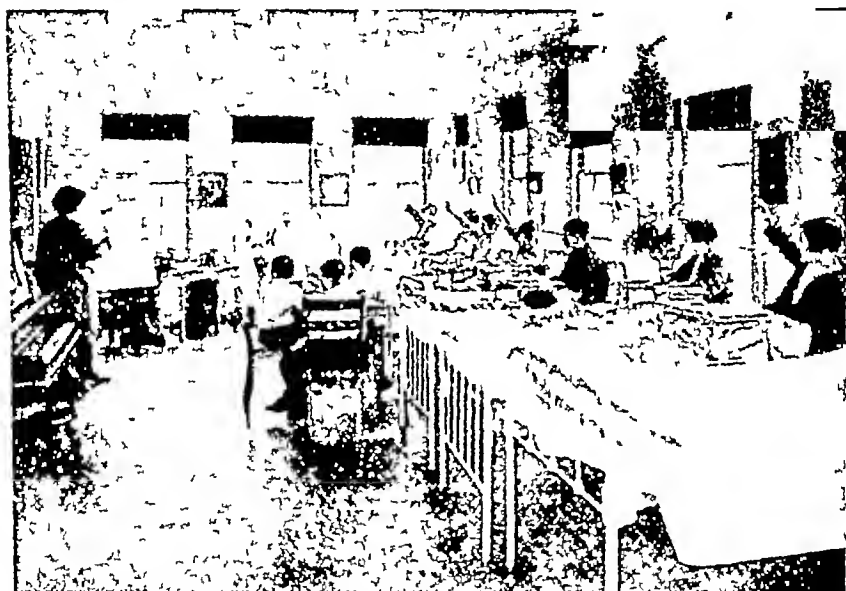
Fig 161 —School room, Children's Heart Hospital of Philadelphia

improvement, is not embraced by this report, for we realize that a five-year period is all too brief for an adequate study of the end-results of rheumatic heart disease which is often characterized by longer or shorter intervals of so-called "latency" between the periods of activity   The evaluation of this feature is as yet somewhat beyond our control   Other variables include, as emphasized below, the influence which the environment into which the child is thrown after his discharge from the hospital may play upon his subsequent course, and as a third important point, we are aware that our attempts to measure the degree of

susceptibility shown by the individual child cannot as yet be accurately measured, but in spite of these variables, several important facts are brought out by these figures

Only those children whose condition falls within the following requirements are admitted to the Children's Heart Hospital

1 Age limit Boys, three to twelve years, girls, three to thirteen years

2 Children shall have either possible or potential cardiovascular disease

Fig 162 —Children's Heart Hospital of Philadelphia and nurses home

3 No patients who have had congestive circulatory failure or with a hopeless prognosis shall be admitted

4 Before admission each child shall spend at least two weeks in a hospital

5 So far as possible all foci of infection should be removed

6 Parents shall agree that children will remain in the hospital from three to six months or longer, at the physician's discretion

The daily routine of the hospital is as follows

TABLE I

DAILY ROUTINE IN CHILDREN'S HEART HOSPITAL

Temperatures	7 to 7 30 a. m
Breakfast	7 30 a m
Older children attend school from	9 to 11 30 a m
Younger children rest from	9 30 to 11 30 a. m
Younger children attend school from ؛	11 30 to 12 30 p m
Older children rest from	11 30 to 12 30 p m
Dinner	12 30 p m , radio
Temperatures	1 to 1 30 p m.
Younger children attend school from	1 30 to 3 p m
Older children play until 2 30 and rest from	2 30 to 4 p m
Younger children rest from	3 to 4 p m
Play hour	4 to 5 15 p m
Temperatures	5 15 p m
Supper	5 30 p m , radio
Bedtime	6 15 p m , radio

The rectal temperature, pulse, and respirations are recorded three times daily, while weekly leukocyte counts and weights are recorded   The children are confined to bed with bathroom privileges for the first few weeks at the hospital   So soon as the rectal temperature stays constantly at 100° F or less, the leukocyte counts are below 10,000, the gain in weight and general clinical condition seems satisfactory, the child is allowed to sit up for fifteen minutes a day   This time is increased by fifteen minutes daily until the child is sitting up for one and a half hours a day for several weeks   If the above four criteria—namely, the temperature, leukocyte count, gain in weight, and general clinical picture—continues satisfactory, the time the child sits up is increased daily by fifteen minutes until the period out of bed reaches three hours a day, when another halt of several weeks' observation is made   Then if improvement continues, the added effort of dressing and being up three hours is allowed during another period of a few weeks observation   If improvement is maintained, the child is allowed after dressing to walk about the wards, carry trays, etc and for the final few weeks stay at the hospital, the child is allowed gradually increasing walks of one-half to one mile   Although of course the individual child's resistance to the rheumatic infection must necessarily determine the rate at which it can be allowed to increase its physical effort, yet the average stay in the hospital per child is about six months

The following tables and most of the conclusions are based upon the report of a follow up study made by the Philadelphia Health Council and Tuberculosis Committee[3] at the request of the Philadelphia Heart Association in the Spring of 1928. The field work was done by Miss Helen G. Wilson, R. N.

There have been 272 children discharged from the Children's Heart Hospital of Philadelphia since its opening day April 24, 1922. Twenty-six children were discharged twice and one child was discharged three times, making in all a total of 300 discharges.

Fig 163 —Rest period on sun porch at Children's Heart Hospital

The first discharge was on July 2, 1922, and the last discharge considered in this study on June 23, 1928. There was only one child in these six years who died while at the hospital. Of the 272 children discharged in these six years, follow up information was obtained from 188 children, 57 being dead on July 1, 1928 and 27 not found.

There were 144, or 53 per cent, of the children who were attending school or working at the time of the follow up. There were 44, or 16 per cent, who were unable to attend school

TABLE I

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Younger children rest from	3 to 4 p m
Play hour	4 to 5 15 p m
Temperatures	5 15 p m
Supper	5 30 p m , radio
Bedtime	6 15 p m , radio

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There were 144, or 53 per cent , of the children who were attending school or working at the time of the follow-up There were 44, or 16 per cent , who were unable to attend school

There were 57, or 21 per cent , who had died and 27, or 10 per cent , whom the worker had not been able to locate

To some, these findings may seem discouraging, yet much comfort may be obtained from a recent report of the Metropolitan Life Insurance Company[4] in which we find the following

"There is, furthermore, a brighter side to this picture of heart disease   When the heart disease mortality data for the various age-ranges are considered, it is found that the rise

Fig 164 —Boys' ward, Children's Heart Hospital

in the deathrate applies only to the higher age groups, and that distinct improvement has taken place, in recent years, in childhood, adolescence, and early adult life—in fact, up to age forty-five, among males, and up to sixty-five, among females   In the United States Registration Area, in 1926, heart disease was responsible for more deaths of children than was scarlet fever, for almost one-half as many as diphtheria, and for two-fifths as many as measles   To our mind, the decline in the cardiac disease deathrate among children will be found, on analysis, to be very largely a reflex of the great strides that have been made in the

TABLE II

Deathrates per 100,000 from Heart Disease (International List Title No 90) Males and Females—by Age

Metropolitan Life Insurance Company Industrial Weekly Premium paying Business 1911 to 1928.

Age Period	1911	1912	1913	1914	1915	1916	1917	1918	1919	1920	1921	1922	1923	1924	1925	1926	1927	1928
MALES																		
1 to 4																		
5 to 9																		
10 to 14																		
15 to 19																		
20 to 24																		
25 to 34																		
35 to 44																		
45 to 54																		
55 to 64																		
65 to 74																		
75 and over																		
FEMALES																		
1 to 4																		
5 to 9																		
10 to 14																		
15 to 19																		
20 to 24																		
25 to 34																		
35 to 44																		
45 to 54																		
55 to 64																		
65 to 74																		
75 and over																		

Rates for 1928 are provisional.

control of diphtheria and scarlet fever, of the increasingly intelligent care that is being given to children who have had infectious diseases, of the earlier diagnosis of rheumatism, of the increase in tonsillectomies and of improved dental hygiene "

Of the 272 children discharged in these six years there were 139 boys and 133 girls   Only three of the children were under five years of age on the date of discharge, 124 were five to nine years old, 137 were aged ten to fourteen years, two were over fifteen, and there were six in which this information was not available

When the 272 children discharged are considered according to the classification scheme used in cardiac clinics, there were 69 in Class I (patients with organic heart disease who are able to carry on their habitual physical activities), there were 76 in Class II, of whom 41 were in Class IIa (patients with organic heart disease who are able to carry on slightly decreased physical activity), and 35 in Class IIb (patients with organic heart disease who are able to carry on greatly decreased physical activity) It is interesting to note that there were 63 children with heart disease serious enough to warrant their being Class III heart cases (patients with organic heart disease who are unable to carry on any physical activity)   In Class E (patients with possible heart disease) there were 21, and in Class F (patients with potential heart disease) there were 39   For the other four the classification was not stated

There were 26 of the children who had been discharged from the hospital since January 1, 1928, 44 were discharged in 1927, 55 in 1926, 36 in 1925, 43 in 1924, 54 in 1923, 14 in 1922

Thus this group of discharged patients represents children with heart disease of all degrees of seriousness   About half were girls and half boys   The age limits were practically from five to fifteen years   The average number of discharges each year was 45

When this evidence of the physical condition of the children is considered according to the age of the child at time of discharge there seems to be little difference between the children under ten years of age and for those over ten   It is interesting to note that there is a decidedly better showing for the boys than for the girls   (See Table III)

When these facts are considered in relation to the heart condition of the children the fact stands out at once that 38 of the

TABLE III

Physical Condition at Time of Follow up According to Age and Sex of the Children

Age and sex	Total children	Children discharged according to physical condition at time of follow-up				
		Able to attend		Unable to attend school or work	Died	Not found
		School	Work			
Total children	272	125	19	44	57	27
Boys	139	68	10	20	26	15
Girls	133	57	9	24	31	12
Under 5 yrs	3	2	—	—	—	1
5–9	104	66	—	22	3	13
10–14	137	56	18	21	31	11
15 and over	2	—	1	—	—	1
Age not stated	6	1	—	1	3	1

Age at time of discharge

63 children in Class III (patients with organic heart disease unable to carry on any physical activity) were dead on July 1, 1928   As might be expected, children in Class I and Class F were more able to be attending school or working than those in the other classifications   (See Table IV)

TABLE IV

Physical Condition at Time of Follow up According to Classification of Heart Condition

Classification of heart condition	Total children	Children discharged according to physical condition at time of follow-up				
		Able to attend		Unable to attend school or work	Deceased	Not found
		School	Work			
Total children	272	125	19	44	57	27
Class I	69	37	6	10	5	11
Class II a	41	23	3	9	4	2
Class II b	35	14	5	7	6	3
Class III	63	12	—	9	38	4
Class E	21	11	4	5	—	1
Class F	39	26	1	3	3	6
Not classified	4	2	—	1	1	—

The facts concerning the medical supervision after discharge of the 272 children were studied   There were 158, or 58 per cent, of the 272 who were under satisfactory medical supervision at the time of follow up   Only 34 of the 158 were under the care of private physicians, the rest being under clinic supervision   "Satisfactory" means in general that the children had been to a physician or clinic within a year and were following the advice given them   There were four who were in hospitals at the time of follow up   It is in the group who were not under satisfactory care that the follow up worker was able to urge a return to the physician or clinic.   There were 30 children in this group, and

the field worker plans to revisit them shortly to find whether her work was successful in getting them under medical supervision again   As has been said, 57 children had died since discharge and 27 could not be located

When the present medical supervision of the children discharged since 1922 is studied according to the length of time since discharge, it is seen that the more recently discharged children are more apt to be under supervision   It is worth noting that there was a particularly heavy mortality among children discharged in 1923 and in 1926   These were also the years of the greatest number of discharges and it may be that in these years new policies were made concerning the length of care and type of cases   It would also appear that in 1924 and 1925 a more satisfactory method of referring discharged children for medical supervision was adopted, as judged by the fact that of the 1924 discharges there were 19 per cent not under medical supervision and in 1925 only 8 per cent   Since 1925 this percentage has been still lower (Table V)

TABLE V

MEDICAL SUPERVISION AT THE TIME OF FOLLOW-UP ACCORDING TO
YEAR OF DISCHARGE

Year of discharge	Total children	Children discharged according to medical supervision at time of follow up					
		Satisfactory supervision		In hospital	No medical supervision (care unsatisfactory)	Deceased	Not found
		Private physician	Clinic				
Total children	272	34	120	4	30	57	27
1928 (6 mo)	26	7	14	1	1	3	—
1927	44	8	27	—	3	4	2
1926	55	3	29	—	4	14	5
1925	36	2	16	1	3	8	6
1924	43	7	16	—	8	6	6
1923	54	7	17	1	7	16	6
1922 (6 mo)	14	—	1	1	4	6	2

There is a better showing for the children under ten, since 61 per cent of them were under satisfactory medical supervision, and 57 per cent of those aged ten or more (Table VI)

When the present medical supervision of the children is considered according to the scheme of classification of the Association of Cardiac Clinics,[5] it is apparent that those in Class F (patients with potential heart disease) are less apt to be under

TABLE VI

Medical Supervision at the Time of Follow up According to Age* and Sex of the Children

Age and sex	Total children	Satisfactory supervision		In hospital	No medical supervision (as unsatisfactory)	Deceased	Not found
		Private physician	Clinic				
Total children	272	34	170	4	30	57	27
Boys	139	15	63	2	18	26	15
Girls	133	19	57	2	1	31	1?
Under 5	3	—	2	—	—	—	1
5–9	124	12	60	3	13	23	13
10–14	13	22	56	—	1?	31	11
15 and over	2	—	1	—	—	—	1
Not stated	6	—	1	1	—	3	1

Age at time of discharge

medical supervision, although the numbers are rather small to permit generalizations However, it would seem necessary to impress upon the patients in Class F the need for medical supervision (Table VII)

TABLE VII

Medical Supervision at the Time of Follow up According to Classification of Heart Condition

Classification of heart condition	Total children	Satisfactory supervision		In hospital	No medical supervision (as unsatisfactory)	Deceased	Not found
		Private physician	Clinic				
Total children	272	34	120	4	30	5?	27
Class I	69	8	38	—	?	5	11
Class IIa	41	7	25	1	2	4	2
Class IIb	35	6	16	3	2	6	3
Class III	63	2	14	—	5	38	4
Class E	21	6	8	1	5	—	1
Class F	39	4	17	—	9	3	6
No stated	4	1	2	—	—	—	1

The general impression, as the worker visited in the homes, was that the children were in a satisfactory condition It would seem that a follow up study in later years will be even more interesting as the children will be older and will have had a chance to show their abilities

Most of the mothers were much interested in talking about their children and had been carefully instructed at the heart clinics in caring for them Those who had taken their children home against advice were sorry and realized that it was a real problem to care for them at home The children receive notices in the majority of cases advising them when to return to the

clinics, and in many cases the worker was visiting in the homes supervising the whole family Though many of these mothers had large families and were very busy, they seemed to feel it their duty and privilege to consider the sick child first

In some of the homes, however, disease seemed to prevail In 15 families there was more than one member attending a heart clinic One case stands out in particular R I , discharged December 13, 1925, a boy now twelve years old, has been admitted to a hospital four times in the two and a half years since his discharge from Wynnefield He has twin brothers—one who at the time of the visit was in a hospital with rheumatic fever, and the other, 11 pounds underweight and very nervous, was attending a heart clinic regularly A sister, twenty years of age, has a heart condition but was able to work The father of the children died of a heart condition The mother has since married, and by the second husband has a two-year-old child, who the mother says is the healthiest child she has ever had

This report, as to the results of treatment of children suffering with rheumatic cardiovascular disease, is offered as a possible basis of comparison for the results obtained with similar patients by the serum-vaccine treatment and the treatment by "intravenous desensitization or immunization with suitable antigenic substances" now in the process of development

In closing I wish to express my gratitude to Dr John R Paul of New Haven for his careful revision and criticism of this report

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CONTRIBUTION BY DR JAMES CRAIG SMALL

FROM THE LABORATORIES OF THE PHILADELPHIA GENERAL HOSPITAL

STREPTOCOCCI IN RELATION TO RHEUMATIC DISEASE

PRACTICALLY all of the recent studies of the rheumatic diseases tend to show that streptococci are intimately concerned in their etiology The manner in which these organisms attack in producing pathologic lesions is quite complex, and at best but imperfectly understood in the present stage of our knowledge We may consider three main methods of attack, any one of which, or the combination of all, or any two of which may operate in the particular case

These are 1 Through the immediate effects of lodgment and growth of streptococci in the tissues

2 Through the action of toxins distributed generally from some local focus of growth of streptococci

3 Through the action of some other bacterial products distributed from a focal source and capable of inducing and maintaining an allergic state of the animal organism

It appears very probable that these three methods of attack seldomly operate singly The simplest combination of them may be outlined as

(a) The effect of the toxins distributed from a primary focal source of infection in producing tissue damage at a distant point, which in turn serves as a prepared location for the secondary lodgment of the bacteria from the primary nidus of infection, or for *other bacteria* happening to gain entrance to and transportation in the body fluids

to the secondary localization of the bacteria from the primary focus, or of other bacteria transported to the site of the allergic lesion

Let us consider briefly these three basic methods of attack

1 **The Actual Lodgment of Streptococci in the Tissues** — Our experience with lesions in which this ordinarily occurs has been that suppuration appears early, and that the identification of streptococci by both smear and culture constitutes a very commonplace bacteriologic procedure   Why then is the demonstration of streptococci such a difficult and inconstant matter in the acutely inflamed joints of rheumatic fever and in certain stages of other arthritides? It is due to the nature of the streptococcus, which lacks virulence, some will say   Yet none are prone to classify the various streptococci obtained in culture from these lesions as any other than pyogenic micro-organisms One of the outstanding features of the local and metastatic experimental lesions produced in animals by such strains has been suppuration   Why the evanescent character of the acutely inflamed joints in rheumatic fever when the usual lesions in which streptococci appear heal out slowly?

In the arthritis produced by localization of the gonococcus in the joints these micro-organisms are easily identified in the very acute stages and become more and more difficult to identify as the arthritis takes on a more chronic form   Why should not these conditions apply in streptococcal arthritis, instead of its being equally difficult to demonstrate the micro-organisms in both the acute and chronic forms of lesions of the non-suppurative type of this disease?

These and many other considerations raise questions difficult to answer and cause one to speculate on the possibility of whether or not the streptococci at times actually recovered from the joint lesions were present locally at the beginning of the inflammatory process, as prime instigators through their immediate irritating effects, or whether they came along as opportunists to find temporary lodgment in foci of lowered resistance to streptococci

2 **The Effects of Toxins of Bacteria** —In the disease caused by true toxins as, for example, diphtheria and tetanus, two

features stand out These are (a) The lack of tissue invasiveness of the bacteria themselves, and (b) the selective action of the toxin on certain tissues known as trophism The local nidus of infection while usually easily identified, is ordinarily a minor consideration among the pathologic lesions established by the disease Toxin formation on the part of a bacterium does not appear to be a factor favoring the opening of tissue spaces for the general dissemination of the bacterium and may actually have the opposite effect

Toxic products of streptococci (endotoxins) are well recognized Among the toxin formers, those of scarlet fever and erysipelas stand out pre-eminently These tend to disseminate their toxins from localized areas of infection Invasion of the organisms is for the most part limited to the regional lymph channels The lesions which kill are usually those produced in more vital organs and structures than those actually invaded by the bacteria

The question of a toxic product generally disseminated enters into any consideration of rheumatic fever The destructive and proliferative lesions in the heart and blood vessels, for example, have never been shown consistently to harbor the actual bacteria May they be accounted for on the basis of the action of a toxin? And, if so, may the acute exudative lesions of the joints, pericardium, and pleura be accounted for on the same basis? These are questions to which definite answers cannot at present be formulated

It is pertinent here, however, to make two observations The first is that joint lesions, as peripheral easily observed exudative lesions in rheumatic fever respond to salicylate medication, concerning the beneficial effect of which on the destructive and proliferative lesions of the heart, there is serious doubt This difference of response in the two types of lesions suggests very strongly that the underlying mechanisms producing them are different

In calling attention to Streptococcus cardioarthritidis[1] as being concerned in the etiology of rheumatic fever, it was shown that an antiserum against its rather subtle endotoxin could be

prepared   In applying this antiserum clinically in rheumatic fever, clinical detoxification of the patient and rapid improvement in the heart action, as evidenced by improvement in valvular tones, the decrease in size of dilated hearts, and the disappearance of the congestion of the liver, were more consistently observed than was a prompt clearing up of the acutely inflamed joints

When more potent antiserum was prepared by the globulin precipitation methods, the decrease in volume dosage naturally led us to practice the administration of more liberal quantities of the antibodies   We then began to observe actual extension of the acute arthritis to new joints closely following and apparently associated with the administration of the antiserum This was spoken of as the "focal reaction" and has also been noted to follow the administration of other antistreptococcal serums in acute rheumatic fever   The explanation of this reaction will be suggested later

It is significant here because the difference in response of the heart and joint symptoms further suggests differences in their pathogenesis

3 Bacterial Allergy —We then come to the third basic method of attack by streptococci—the question of bacterial allergy   This is the newest and its significance perhaps the least understood   We are handicapped in our interpretations here because we lack an understanding of fundamental basic principles underlying the hypersensitive or allergic state and its relation to immunity   A great deal of confusion will be avoided at the start if we appreciate the fact that the capacity of antigens for inducing specific allergic states in animals depends more particularly on their chemical composition than it does on their biologic origin, as was demonstrated by Wells and Osborne[2] in their work on purified vegetable proteins   Swift's[3] excellent work on allergy to streptococcus antigens amply demonstrates that these states in animals cross the bars of immunologic type specificity of the bacteria   Birkhaug[4] confirms this and shows further that animals rendered hypersensitive to antigens of streptococci are also hypersensitive to those of pneumococci

Opie[5] in studying the Arthus phenomenon presented evidence to indicate that the hypersensitive state in rabbits induced by injections of crystalline egg albumen and by horse serum, was rather intimately related to the titer of precipitins for these antigens in the animal's serum

Von Dungern[6] brought forth evidence to show that such substances as horse serum and egg white, contain a multiplicity of protein substances, each of which acts as antigen for the production of its own specific precipitin, but that these precipitins do not appear in the blood serum of the immunized animal in the same relative proportions in which the antigens occur in the horse serum or in the egg albumen Dochez and Stevens,[7] and Birkhaug[8] have shown that multiple states of hypersensitiveness exist in animals inoculated with streptococci, one at least of which appears species specific, the other not

The lack of species specificity in the allergic states induced by experimental means with antigens of streptococci has led me[9] to make the suggestion that streptococci and perhaps pneumococci contain a highly organized common protein, which acts as a "specific allergen," regardless of its biologic origin In considering the part which bacterial allergy plays in disease it must not be forgotten that biologic specificity of the infecting bacterium is reasonably regarded as a most important factor in lending clinical and pathologic definition to an infectious disease This is true even within the streptococcus group as is readily appreciated if we consider two such diseases as scarlet fever and erysipelas If we disregard this we are striking a deadly blow at the specificity of bacterial disease in its broadest aspects Do patients with the arthritis of rheumatic fever and with other forms of subacute and chronic arthritis, exhibit hypersensitiveness to the products of streptococci? The answer to this is easily found upon the injection of minute doses of the saline extract of streptococci into such patients Focal reactions in the joints and general reactions clearly signify that they are If the saline extract is injected into normal individuals, these reactions do not occur If the extract is boiled for two hours, the reactions are still manifest upon injection into arthritics

The logical deduction is that a bacterial toxin is not concerned
If extracts of widely different types of streptococci are used,
identical reactions are obtained in patients with chronic ar-
thritis

There is no doubt but that such individuals exhibit extreme
grades of hypersensitiveness to products of widely different
types of streptococci   These reactions in chronic arthritis
(infectious type) are commonly elicited with doses in which the
amount of bacterial protein as calculated is about one 20 billionth
of a milligram   I do not know of any more outstanding example
of hypersensitiveness in medical practice than this

While these states exist in a disease condition, we must not
be too prone to regard them as the one and only factor concerned
in the various manifestations of the disease   They in no meas-
ure militate against the conception of a toxin as being concerned
as well in the disease   An example cited by Neil[8] emphasizes
this   He records a case of hypersensitiveness to some protein
factor of the diphtheria bacillus which showed cross sensitization
to certain non-toxic allied bacilli as well   This hypersensitive
state was in no way related to susceptibility or immunity to
the toxin of the diphtheria bacillus   Any symptoms arising,
therefore, as a result of this hypersensitiveness could not be
regarded as clinical diphtheria   Neither can the allergic symp-
toms in rheumatic fever be regarded as the whole story in this
disease, even should they occur in every case

On the other hand, the allergic symptoms do not occur with
significant intensity in all cases of rheumatic fever   In evidence
of this we need only call your attention to rheumatic fever in
childhood without joint symptoms as contrasted with the ordi-
nary adult type of the disease with joint symptoms, and to the
futility of salicylates in the former as contrasted with the
apparent success in the latter   Salicylates tend to offset the
allergic states in experimental animals   The deduction, there-
fore, again appears logical that the exudative lesions in rheu-
matic fever are manifestations of allergy and that they are on a
different basis from the destructive and proliferative cardiac
lesions

We should not lose sight of the influence which both or either a toxin and the allergic state may have in preparing the soil for the focal growth of streptococci in the inflamed tissues, but it need not necessarily follow that the streptococci which are predetermined to these lesions are of the particular species providing the toxin or the allergen. In subacute bacterial endocarditis as a complication of rheumatic endocarditis, we have an outstanding example of the entrance of a new type of streptococcus to grow in tissue damaged by the toxic or allergic effects of its predecessor.

As a development of our studies of rheumatic fever during the past two years in which the antiserum and antigen of Streptococcus cardioarthritidis have been used extensively in the treatment of clinical cases, a working hypothesis has been developed. This may be stated briefly as follows.

The "destructive" and "proliferative" lesions of rheumatic fever (blood vessel and cardiac lesions) are produced by a different mechanism from that causing the exudative lesions (acute arthritis).

The former types of lesions are produced by the action of a specific toxic product (endotoxin) derived from a particular specific streptococcus. The latter type of lesion arises because of the establishment in the patient of a condition of hypersensitiveness to a protein fraction contained in streptococci and is a manifestation of the Arthus phenomenon. This protein fraction is a highly specialized protein common to quite diverse immological strains of streptococci. It acts as a "specific allergen" because of its chemical structure and regardless of its biologic origin.

This conception does not disturb the specificity of the "destructive" and "proliferative" cardiac lesions of rheumatic fever, but does indicate that the exudative arthritic lesions may depend upon bacterial "protein" specificity regardless of the strain of streptococcus supplying the particular protein in question. This non specificity of the allergic factor as to serological type of streptococcus may not limit the arthritic involvements to a single specific streptococcus. The rheumatic carditis, how-

ever, would be limited to a single specific streptococcus, because of the biologic specificity of its endotoxin

The problem in therapy of acute rheumatic fever appears to be that of complete neutralization of the toxic factor by a specific antiserum without passively transferring to the patient hypersensitization to the protein antigen common to different streptococci The "focal" reaction in the joints following the injection of the antiserum of Streptococcus cardioarthritidis[1] in patients with acute rheumatic fever appears to be a manifestation of this passive transfer of allergy To avoid this it would become necessary to remove from the antiserum the antibodies of the protein fraction of the streptococcus without destroying its effectiveness by the removal of any of its antitoxin content

CHRONIC ARTHRITIS

The relationship of those forms of chronic arthritis variously spoken of as atrophic, hypertrophic, rheumatoid, and deforming arthritis to the arthritis of rheumatic fever, is but poorly understood That there is a relationship has appeared very early in our work upon the clinical trials of the antiserum, vaccines, and soluble antigens of Streptococcus cardioarthritidis in such patients

Well-marked general reactions accompanied by focal activation of the joints in patients with these forms of chronic arthritis followed the injection of small doses of the vaccine prepared from this streptococcus When the reactions were shown to occur following the subcutaneous injection of doses as small as that represented by 50,000 of the killed streptococci, it was decided to employ only the saline extracts of the bacteria as a means of reducing and of more accurately regulating the dosages to be employed

The bacteria, washed free of the fluid medium in which they were grown, were suspended in normal saline in a concentration of 100 millions per cubic centimeter After a period of seven days in the refrigerator, the bacteria are removed by filtration and the water-clear saline extract only is preserved for therapeutic use This extract, spoken of as soluble antigen, must

be further diluted with normal saline for clinical use. At present three dilutions of it are being used. These are represented by 1 to 1 million, 1 to 10 million, and a 1 to 100 million dilutions of the above extract. Following the injection of as little as 1/20 c.c. of the 1 to 100 million dilution in patients with chronic arthritis definite general and focal reactions arise. When one considers that this amount represents 1/20 of the saline extract of a single streptococcus, the extreme hypersensitiveness of this type of patient to the product immediately becomes apparent

This type of therapy at once strikes one as being very different from vaccine therapy. The important differences are

1. Only individuals suffering from chronic arthritis show reactions to such small amounts. Normals are insensitive to them

2. The small amount of antigen in the dosage used would not be considered sufficient to be efficient in building antibodies

3. Individuals reacting to the unheated antigen will also respond to antigen which has been boiled for two hours so that an ordinary bacterial toxin does not enter as a factor

4. Antigens prepared from streptococci of widely different characteristics elicit corresponding responses in the patient with chronic arthritis

On the basis of these considerations we have come to regard these forms of chronic arthritis as manifestations of the extreme hypersensitization of the individual to certain products of streptococci. These products are not endotoxins since boiling the antigen for two hours or varying the type strain of streptococci from which the antigen is prepared does not materially affect the type or severity of the individual's reaction. They suggest very important considerations bearing on the etiology and pathogenesis of chronic non-suppurative arthritis. First, that the disease need not be produced by a toxin forming, pathogenic streptococcus. Second, the lack of strain specificity in these reactions to antigen renders it probable that a great many varieties of streptococci have the property of inducing a hypersensitive state, which manifests itself as chronic arthritis in patients. Third, the relatively inert streptococcus growing in a focus of infec

tion so insignificant as to escape detection clinically, may yet
be responsible for the chronic arthritis, through its supplying
for dissemination minute amounts of soluble non-toxic strep-
tococcal products which act as sensitizing agents

From the standpoint of therapy, the problem in chronic
arthritis, we believe, is that of desensitization, rather than that
of building up specific resistance to a particular streptococcus
identified in a focus as the probable offender in a particular case
Two things are necessary in this form of treatment

1 Removal or elimination of closed foci harboring strepto-
cocci, so as to be rid of such foci as reservoirs for supplying the
sensitizing products

2 Treatment with carefully regulated small amounts of the
soluble products of streptococci, in a course of injections for
"desensitizing" the patient

The dosage of the soluble antigen, the method of injection,
and the time intervals between injections are more important
considerations by far than is the type of streptococcus from
which the antigen is prepared

We have employed extremely small doses injected subcuta-
neously at four- to seven-day intervals   The dosage is very
gradually increased as a tolerance for it appears to be estab-
lished, and the interval is prolonged with the larger doses
Our schedule of dosage for the soluble antigen of Streptococcus
cardioarthritis is

Dilution 0 1 100,000 000	Dilution 1 1 10 000,000	Dilution 2 1 1,000,000
0 05 c.c		
0 07 "		
0 10 "		
0 15 "	0 15 c.c	0 15 c c
0 25 "	0 25 "	0 25 "
0 35 "	0 35 "	0 35 "
0 5 "	0 5 "	0 5 "
0 7 "	0 7 "	0 7 "
1 0 "	1 0 "	1 0 "

A given dosage should not be increased as long as it elicits
general or focal reactions, affects the pulse-rate, tends to lower
blood-pressure, or is attended by a loss of body weight

The last two considerations are most important because it is often difficult where a patient is suffering greatly from arthritic pains to determine whether or not these have become worse following an injection

While well aware of the experimental evidence in animals that intravenous administration of antigen is the most effective method of bringing about desensitization we have not employed it extensively in patients under this treatment In the majority of cases such considerations as advanced age feebleness myocardial weakness, kidney disease cause one to hesitate over employing any form of intravenous therapy

In suitable cases after the subcutaneous injections have been continued for some time, we have used intravenous injections, but as yet have insufficient data to formulate any comparison of these results with those following subcutaneous administration

Thus our hypothesis in regard to chronic arthritis differs essentially from that mentioned in regard to acute rheumatic fever, but chiefly in one particular, namely, that a specific biologic toxin of streptococci is not a factor in the pathogenesis of chronic arthritis Foci harboring streptococci are regarded as distributing non toxic sensitizing antigens which appear to be common to many varieties of streptococci Chronic arthritis arises not because of infection with a particular type of streptococcus, but because of the hypersensitive state induced by an "allergen" common to many types of streptococci

In rheumatic fever this same type of allergy exists, but the essential lesions of the disease are not in the joints but in the blood vessels and heart These latter are regarded as arising from the effects of a specific biologic toxin which appears to have a selective action on endothelial tissue Of the two types of disease, rheumatic fever is much more complex than is chronic arthritis because of the multiple factors involved in the several types of pathologic lesions

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SPONTANEOUS SUBARACHNOID HEMORRHAGE

DURING the past year, 3 patients were admitted to the Medical Division of the University Hospital, in whom the diagnosis of spontaneous subarachnoid hemorrhage was made The paucity of medical literature on this subject in this country has been deprecated by the few American authors who have written on it particularly by Samuel Leopold[1] in 1914 and Josephine Neal[2] in 1926 Suffice it to say, that the most comprehensive contribution by C P Symonds[3] of Guy's Hospital in 1924, contains 77 references to current literature, only a single one of which was published in this country

Subarachnoid hemorrhage may result from a great variety of causes It may occur in various types of meningitis particularly syphilitic, tuberculous and meningococcic. It may occur as the result of a blood dyscrasia and has been observed in hemophilia purpura, and leukemia Bleeding into the subarachnoid space may arise from rupture of an embolic intracranial aneurysm which has developed during the course of malignant or subacute infectious endocarditis Recently a patient has been seen in whom hemorrhage into the subarachnoid space resulted from the rupture of a cerebral cyst into the lateral ventricle Trauma of course may be the cause The reasons for subarachnoid hemorrhage in most of these cases are obvious, inflammatory processes, deficiency in factors concerned in coagulation and accidental causes

There are however, other instances of subarachnoid hemorrhage in which all of these factors can apparently be excluded, and to this group the term "spontaneous" has been applied

Etiology —The frequent occurrence of spontaneous sub-arachnoid hemorrhage in young and otherwise healthy individuals has occasioned the greatest amount of interest in the etiology and pathology of the disease The word *spontaneous* excludes all cases resulting from trauma, specific infections, and blood dyscrasias This leaves only arterial disease and arterial aneurysms of non-bacterial origin to be considered

In regard to arterial disease it would appear at first thought that arteriosclerosis would be the commonest cause, but the age incidence of spontaneous subarachnoid hemorrhage is in striking contrast to that of cerebral hemorrhage, the chief cause of the latter admittedly arteriosclerosis

In Neal's[2] series the average age of 20 cases was twenty-seven years In Symond's[3] series of 114 cases compiled from the literature 39 of undetermined etiology averaged thirty years of age

It appears therefore, that although arteriosclerosis may produce spontaneous subarachnoid hemorrhage the early age incidence of this disease is strong evidence against its being the usual etiologic cause

The possibilities of vessel rupture in the absence of arteriosclerosis atheroma, and aneurysm have been considered by Parkes Weber[4] who quotes Reuterwall[5] The latter recorded careful examinations of the basilar artery in 82 autopsies, in 7 he found transverse rents in the internal elastic lamina which during life had undergone connective-tissue repair In this series the age incidence ranged from thirty-eight to seventy years

Symonds[3] believes that the Continental writers have not paid sufficient attention to the rôle played by aneurysm in the etiology of this condition

In 1859 Sir William Gull[6] stated, "whenever young persons die with symptoms of ingravescent apoplexy and after death, large effusion of blood is found, especially if the effusion be over the surface of the brain in the meshes of the pia mater, the presence of an aneurysm is probable "

The extreme rarity of syphilis as a cause has been empha-

sized particularly by Turnbull[7] and Fearnsides,[8] in fact neither author believes that syphilis is ever a cause of intracranial aneurysm

Fearnsides[8] recorded 44 cases of aneurysm of the cerebral arteries in 5432 autopsies at the Pathological Institute of the London Hospital between 1907 and 1913 of which 13 were the result of infective emboli and 31 of medial degeneration In 15 of the latter whose average age at the time of death was thirty eight years, no other evidence of cardiovascular disease was observed None was regarded as syphilitic in origin in striking contrast to aortic aneurysms 96 2 per cent of which were due to syphilis, and to arterial aneurysms of vessels other than those of the brain and aorta, all of which were of syphilitic origin

Harvey Cushing[9] in 1923, recorded 5 instances of intracranial aneurysm 4 of which had ruptured and were found at autopsy A single case operated for suspected brain tumor was found to have a pulsating aneurysm

The ages of these 5 cases ranged from twenty-six to fifty two years Only 1 of the 4 proved at autopsy was diagnosed during life This patient was studied by Symonds who was visiting Cushing's Clinic at that time and furnished the impetus for Symonds' future contributions to this subject

From these facts it may be inferred that intracranial aneurysms in young persons are not uncommon and that they hardly ever are due to syphilis Whether they are congenital or result from congenital weakness in a localized area in the arterial wall in the absence of embolic infection is a matter of speculation, that they are found postmortem is certain

Numerous writers have cited instances of 2 or 3 attacks of spontaneous subarachnoid hemorrhage in the same individual Some of these patients have been found postmortem to have small aneurysms, presumptive evidence that rupture of a small aneurysm may heal

It has been assumed that hemorrhage may occur from a functional vasomotor disturbance of the vessels in the sub arachnoid region, analogous to that which is supposed to occur

in Raynaud's disease and in certain cases of migraine, especially since the latter has been a rather frequent symptom long before the onset of hemorrhage   Perhaps this vasomotor disturbance may occur in heat stroke and explain the recorded instances from that cause

That a functional vasomotor disturbance is not a frequent cause is certain, the sudden onset of symptoms and their rapid progression are evidence of a more fulminating process

Symptoms —The symptoms which result from hemorrhage into the subarachnoid space result from increased intracranial pressure, and extravasation of blood into a serous cavity

If the hemorrhage be small and if it ceases promptly there is little increase in general intracranial pressure, so that only headache, vertigo and vomiting may occur   There is sometimes a brief loss of consciousness, even if the hemorrhage be small, which has been attributed to the actual shock of vessel rupture, comparable to the brief unconsciousness which may occur in cerebral concussion   This symptom was not observed in our cases   Symonds[5] comments on the frequency with which the patients state, "something seemed to snap at the base of my skull "   One of our patients "suddenly felt as if he had been hit with a hammer behind the right ear "   If the hemorrhage be large and if it continues, coma and rapid death may ensue

The symptoms and physical findings resulting from sudden extravasation of blood into a serous cavity, are those of meningeal irritation, perhaps indistinguishable from meningismus or meningitis   Moderate fever is the rule, comparable in all respects to that produced by sudden hemorrhage into any serous cavity

Diagnosis —The diagnosis of subarachnoid hemorrhage depends on 3 facts, previous knowledge of its existence, its symptoms briefly those of increased intracranial pressure and meningeal irritation, and on the examination of the spinal fluid The diagnosis of *spontaneous* subarachnoid hemorrhage is made by excluding all of the well-recognized causes of intracranial hemorrhage, trauma, rupture of an intracranial cyst, tumor, acute and chronic meningitis, malignant and subacute infec-

tious endocarditis, sometimes producing intracranial mycotic aneurysms and diseases of the blood per se

From[*] in 1904 described the spinal fluid in subarachnoid hemorrhage so comprehensively that subsequent writers have been unable to do more than confirm his observations   He stated that the spinal fluid usually was under increased pressure and that it was uniformly mixed with blood   On standing no coagulum formed but the red cells settled to the bottom leaving a supernatant fluid in which xanthrochromia developed Where blood is present from accidental contamination, the spinal fluid obtained in 3 or more tubes successively is not uniformly blood tinged, a coagulum forms and yellowish discoloration does not develop in the supernatant fluid

From further stated that the supernatant yellow fluid reacted positively for bile pigment and that *pari passu* with this hemolysis there is an increase in the bile pigment in the blood and urine   In 1926, Parkes Weber[4] applied the van den Bergh test for bilirubin to the cerebrospinal fluid from a case of subarachnoid hemorrhage and found an increase in the indirect reaction.   In this same patient the indirect reaction in the blood serum was also above normal

It is a common experience in hospital practice to encounter the idea that hemorrhagic spinal fluid usually results from contamination at the time of spinal puncture

Knowing this and realizing the difficulties in any particular case despite the criteria established by From, we seized upon the van den Bergh test hoping that it would help us settle the question of true hemorrhage versus hemorrhage from contamination

Accordingly, a series of van den Bergh tests were made of spinal fluid after the addition of blood in vitro and through the courtesy of Dr Frazier and Dr Müller, 19 hemorrhagic spinal fluids were obtained from recently operated brain tumor cases and unoperated patients with fractured skulls where there was no reasonable doubt that the blood in the fluid resulted from intracranial injury

This experimental work is not complete   It will be presented in due course, with simultaneous observations on the bilirubin

content of the blood plasma and certain studies now in progress relative to the bilirubin content of hemorrhagic effusions in other serous cavities   Suffice it to say, that we have no evidence yet to confirm Parkes Weber's observation that the van den Bergh test is capable of distinguishing pre-existing hemorrhage from that of accidental contamination in the spinal fluid

The following cases illustrate the symptoms, signs, and spinal fluid findings previously described

Case Reports —*Case I* —Male, colored, aged thirty-one, while laughing very heartily on November 20, 1927 was suddenly seized with an intense occipital headache   He did not lose consciousness   The next morning he was sent to a nearby hospital where he became delirious and required large doses of morphin for relief of intolerable headache   Three spinal punctures were done, each with temporary relief of headache   The fluid was blood tinged *but this was regarded as being due to accidental contamination*   He was admitted to the University Hospital on December 1st   On physical examination the blood-pressure was elevated, systolic 160, diastolic 75, temperature 99, pulse 48 and respiration 16   The patient was drowsy and stuporous, and the neck was rigid   The reflexes were slightly exaggerated with an abortive ankle-clonus on the right side   The blood Wassermann was negative   A roentgenogram of the head by Dr Pancoast showed slight convolution atrophy in the frontal region   Spinal puncture on December 3d revealed grossly hemorrhagic fluid—two days later it was xanthochromic, and subsequent specimens on December 8th, 9th, 12th, and 15th were similarly tinged   Wassermann tests on the spinal fluid were negative   The van den Bergh test on the blood-serum on December 17th gave a negative direct reaction and an indirect reading of 1 8 units   No van den Bergh test was made on the spinal fluid   There was never any clinical evidence of jaundice   On December 19th the patient was free of headache and symptomatically well   He was discharged on December 24, 1927

Case II —Male, white, aged forty-one, was admitted to the service of Dr Alfred Stengel on December 29, 1927   On the day

of admission there developed without apparent cause, an in
creasingly severe occipital headache which became so intense
while running for a street car, that he had to stop and sit down
He was found sitting on the pavement and brought to the hos
pital   The previous medical history revealed an interesting
story   He had previously been admitted to the University Hos
pital at the age of sixteen years, in 1903   While in the hospital
at that time his chief complaints were headache and backache
The pulse was slow, and there was a moderate fluctuating tem
perature for twelve days with a leukocyte count ranging from
12,000 to 18,000   A diagnosis of serous meningitis was made
Recovery was complete and uneventful   There was no examina
tion of the spinal fluid   On admission December 29, 1927 he
complained of intense headache   The mental state was normal
Nothing of note was found on routine physical examination and
neurologic examination revealed nothing abnormal   The first
specimen of urine contained a trace of sugar—the fasting blood
sugar was normal   The blood Wassermann was negative
Spinal puncture was done on December 31st, the fluid was under
increased pressure and was uniformly blood tinged   Similar
fluid was removed on January 3d   On January 5th the fluid
had become xanthochromic   The Wassermann on the spinal
fluid was negative

x Ray examination of the head by Dr Pancoast showed cal
cification in the region of the right choroid plexus, with atrophy
of the dorsum sellae and posterior clinoids, suggesting increased
intracranial pressure   The unilateral calcification in the region
of the choroid plexus was regarded by Dr Pancoast as suspicious
of calcification within an intracranial tumor in the right temporo
parietal region

This report suggested the diagnosis of cerebral neoplasm but
there were no confirmatory focal or ocular signs of tumor   In
view of the fact that the previous illness in 1903, diagnosed
serous meningitis, might well have been a previous subarachnoid
hemorrhage, cases with recurrence are not uncommon, it was
thought by Dr N R Clarke, the intern on the ward, that the
calcification demonstrated in the roentgenogram might have re-

sulted from the previous hemorrhage at the age of sixteen   The patient was discharged symptomatically well on January 17, 1928

Case III —Male, white, aged seventy, was admitted to the service of Dr Alfred Stengel on September 21, 1928   On September 17th he suddenly "felt as if he had been hit with a hammer behind the right ear " Severe frontal headache ensued   On physical examination the peripheral vessels were markedly sclerotic   There was a slight rigidity of the neck   The heart was enlarged to the left and there were numerous extrasystoles   A bilateral Babinski was present   The blood Wassermann was negative   Spinal puncture on September 22d revealed grossly bloody fluid   The spinal fluid Wassermann was negative   The spinal fluid on September 25th was bloody and on October 13th it was xanthochromic   On November 2d the fluid was clear   The van den Bergh test on this fluid showed a negative direct reaction and an indirect reaction of 0 2 units   On October 10th the blood serum van den Bergh showed a delayed direct reaction and an indirect reading of 0 9 units   There was no clinical evidence of jaundice   On November 2d when the spinal fluid was clear, the van den Bergh test on the blood serum was normal   The patient was discharged free of symptoms on November 2, 1928

In regard to the ophthalmologic findings, in Case I Dr Holloway's examination showed a weakness of the right external rectus muscle and a distinct bitemporal pallor of the fundi, Case II was normal and Case III examined by Dr A G Fewell showed advanced retinal angiosclerosis   None of these patients showed subretinal hemorrhage, which has frequently been described in subarachnoid hemorrhage and which results from extravasation of blood along the sheaths of the optic nerves subsequently to appear under or rupture through the retina

Herpes zoster was not observed, two instances of which have been described by Adie[10] resulting from extravasation of blood into the spinal subarachnoid space

Massive albuminuria has been recorded by Widal[11]

Schneider[1] and others as a striking and sometimes confusing occurrence in subarachnoid hemorrhage   They believe that there is adequate experimental evidence to justify the state ment that this condition may result from lesions of the floor of the fourth ventricle, analogous to the puncture diabetes of Claude Bernard

While transient glycosuria with a normal fasting blood sugar was found in one of our cases, there was no instance of massive albuminuria

Prognosis—The prognosis of spontaneous subarachnoid hemorrhage depends on the cause of the hemorrhage its mag nitude, its duration, and its recurrence

In those cases where hemorrhage results from sunstroke or presumably from some vasomotor disturbance, the extravasa tion is small, and recovery may be expected when increased intracranial pressure is relieved by spinal puncture   Those which occur during youth, presumably due to congenital weak ness of the arterial walls or rupture of small aneurysms, probably congenital, frequently recover, although recurrence is not un common

In older patients where advanced arteriosclerosis is pre sumably the cause, and the hemorrhage therefore is not "spon taneous" particularly if these arteriosclerotic changes produce acquired aneurysms which subsequently rupture, the prognosis is extremely unfavorable

Treatment—From what has been stated, it is apparent that spinal puncture is indispensable in diagnosis   It is equally in dispensable in treatment   If the hemorrhage has ceased prior to puncture, and if the intracranial pressure can be relieved, it is life saving   Theoretically the sudden relief of intracranial pressure may predispose to further hemorrhage, but this is a justifiable risk because if the hemorrhage be massive or con tinuous the prognosis is extremely grave   In our cases striking relief of headache was observed and perhaps life itself was preserved by its use   Other methods of reducing intracranial pressure, particularly the intravenous use of hypertonic glucose, may be of value

The 3 patients with subarachnoid hemorrhage, whose histories have been presented, all recovered   Their etiology therefore must remain obscure   If one is permitted to draw deductions by comparison and analogy we may assume that the disease in Cases I and II, in view of their ages, the absence of concomitant diseases, and the absence of evidence of degenerative cardiovascular disorders, probably resulted from rupture of a small intracranial aneurysm which healed   There is evidence in Case II that hemorrhage occurred first at sixteen years of age, subsequently at forty-one   We believe that these 2 patients are illustrations of spontaneous subarachnoid hemorrhage

The age of Case III, the obvious evidences of cardiovascular disease and advanced arteriosclerosis are indicative of hemorrhage from an arteriosclerotic intracranial vessel   Aneurysmal rupture cannot be excluded, but this occurrence at the age of seventy, in the presence of marked sclerosis, would probably have been fatal

Summary —1 Spontaneous subarachnoid hemorrhage implies sudden extravasation of blood into the subarachnoid space, in the absence of trauma, specific infection, disease of the blood per se, or accidental hemorrhage into the subarachnoid space by way of the lateral ventricles secondary to deep cerebral injury

2 The symptoms, signs, and spinal fluid findings are cited, with particular reference to the possible value of the van den Bergh test for bilirubin, as a method of distinguishing between true and accidental hemorrhage into the spinal fluid

3 The case histories of 3 patients are presented in 2 of whom the diagnosis of spontaneous subarachnoid hemorrhage seemed proper because of symptoms, signs, and spinal fluid findings characteristic of this condition

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AN ANALYSIS OF CARDIOVASCULAR-RENAL DISEASE FROM THE STANDPOINT OF ACCURATE DIAGNOSIS

THIRTY FIVE years ago Sir Clifford Allbutt published the first of a number of papers which established a basis for a clearer conception of essential hypertension and arteriosclerosis In spite of an increasing knowledge of the hypertension problem since that time and additional information regarding kidney disease gained by better methods of blood chemical analysis the clinicopathologic pictures of hypertension, nephritis, and arteriosclerosis are still confused in the minds of the profession in general Indeed, the renal division of this subject is in a special state of confusion

Beginning with a pathologic classification of nephritis from the time of Bright we were forced after the advent of better blood chemical methods to adopt a clinical grouping based upon disturbed renal function During this later period clinicians minds have been divorced from the pathologic basis of kidney disease and students have been taught that it is impossible to correlate the clinical and pathologic findings in nephritis This is a very unsatisfactory state of affairs and because of the confused nomenclature of nephritis and this bad teaching students and practitioners of medicine very freely confess their inability to understand the problem of kidney disease Recently there has been a definite tendency to return to a pathologic classification suggested by the German workers Volhard and Fahr It is significant that American text books of pathology and medicine are each year, in increasing numbers, adopting this classification which is based upon etiology and pathogenesis as

much as upon anatomical alterations and in my opinion indicates a very wholesome tendency in regard to the present-day conception of kidney disease The harassed medical student of today suffers, however, because he is in this transition period, some of his teachers and texts offer him an old time pathologic classification (chronic parenchymatous and chronic interstitial nephritis), others insist upon a clinical grouping determined by evidences of disturbed function (nephritis with nitrogen retention and nephritis with water retention), and still others are beginning to divide the subject, according to the teachings of Volhard and Fahr, into nephritis, nephrosis, and arteriosclerosis of the kidney

This discussion today has to do chiefly with the individual of middle life, generally overweight, who has high blood-pressure, albuminuria, and frequently edema, and who complains of shortness of breath, headache and dizziness, and digestive disturbances The clinical picture of an edematous individual with high blood-pressure, sitting up in bed puffing for breath is a common one both in private and hospital practice, and is the type of case that is loosely called cardiovascular-renal disease The employment of such an inexact term connotes loose thinking on this subject and as a consequence leads to unsatisfactory treatment and bad judgment in prognosis

Due to a better understanding of the nature of the hypertension process, to better methods of estimating kidney function, and to a general adoption of a more satisfactory classification of nephritis I believe we now are in a position to adequately analyze these cases giving a more accurate diagnosis based upon etiology and pathogenesis, anatomic change and functional derangement

A patient with hypertension and albuminuria may fall into any one of several groups, viz

1 Essential hypertension

2 Essential hypertension which has progressed into chronic nephritis

3 Cardiac disease with renal congestion

4 Chronic glomerulonephritis

Because of high blood pressure slight albuminuria or retinal changes discovered by an ophthalmologist (many of whom still confuse the findings in hypertension arteriosclerosis and nephritis although the advance in knowledge of pathologic alterations in the eye ground has kept pace with our general understanding of vascular disease) the individual with essential hypertension has been told too frequently in the past that he suffers from "Bright's disease" and as a result lives a life of invalidism in the expectation of a death from uremia which rarely comes We have made little advance in our understanding of the cause of essential hypertension but we have progressed far in our knowledge of its course and its effects upon the various organs and tissues The life history of the hypertension process might be briefly sketched in the following fashion

As to etiology we presume there is much in heredity for we are all familiar with the increased incidence of high blood pressure, apoplexy, heart failure, and kidney disease in the family histories of such patients Many close students of the subject believe that the stigmata indicating potential hypertensive disease are disturbances of the autonomic nervous system manifested by signs of vasomotor instability during the early years of the individual A little later, that is during the 20's or 30's there occur periods of hypertension with a quick return to normal following rest and relaxation. During middle life there is a sustained hypertension with failure to return so promptly to normal following rest Later during the 50's and 60's the evil effects upon the organs, especially the arteries, heart, and brain are manifested, and having withstood the hypertension for a period of fifteen or twenty years the individual finally succumbs to heart failure, apoplexy, or in a small percentage of cases to renal disease

In perhaps 10 per cent of instances the process that we have just discussed, essential hypertension, eventuates in chronic nephritis Differentiation which determines prognosis and treatment is based upon the results of renal functional tests An individual with hypertension presents himself for examination, perchance there may be a trace of albumin in the urine Tests

of renal function aid materially in determining whether the kidneys are affected to what degree, and what the treatment shall be, continued observation with renal functional tests gives an indication as to prognosis   If these tests, namely, two-hour-specific-gravity tests, the excretion of phenolsulphonephthalein and the blood-urea are within normal limits and remain so, the slight albuminuria may safely be disregarded and the individual considered not from the standpoint of "chronic Bright's disease" but as an instance of essential hypertension   If, however, these various tests show a disturbance of function and this disturbance of function is progressive the probabilities are that chronic nephritis has resulted and that the end will be determined by renal failure

Another and more frequent probability is that myocardial failure will be brought about as a result of persistent hypertension   After years of high blood-pressure the patient shows thickening of peripheral vessels and enlargement of the left ventricle and eventually has myocardial failure   This manifests itself by shortness of breath, edema, and albuminuria   Frequently in spite of a certain degree of heart-failure the hypertension is long maintained   This is the type of case most frequently dubbed "cardiorenal "   The renal element often is given credit for more mischief than it has actually done, and the proof of this becomes apparent when after rest and digitalis edema disappears and albuminuria clears as renal congestion is relieved   The following case is illustrative

C B , a white man was first seen April 28, 1924   He complained of shortness of breath, cough, and swelling of the legs   The family history and past history had no bearing on the present illness   This had begun about ten days previously with an attack of shortness of breath following moderate exertion   Then came cough and swelling of the ankles   The patient continued to work until April 25th when he was forced to go to bed

Physical examination showed a well-nourished white man with moderate dyspnea and cyanosis of the lips   The pulse-rate was 108   The heart seemed somewhat enlarged although the rounded chest made this difficult to determine   A tender liver

edge could be felt two fingerbreadths below the costal margin in the right mid clavicular line   There was no evidence of fluid in the abdomen   The ankles were moderately swollen   The urine on admission showed a cloud of albumin   many white blood cells, was positive for blood and contained numerous hyaline and granular casts   The blood urea nitrogen was 17 mg   The blood-count was good, the blood Wassermann negative   Eye-ground examination was negative   The blood pressure during a months' stay in the hospital averaged about 170 systolic and 90 diastolic   The electrocardiogram showed normal conduction but indicated left ventricular hypertrophy, and the x ray of the chest disclosed a heart slightly larger than normal

The patient improved greatly with rest and digitalis and upon discharge no longer showed dyspnea or edema   The urine contained only a faint trace of albumin and a few white blood cells but no casts or blood, and renal functional tests gave a good response.

The patient was followed after discharge from the hospital and never had a return of congestive heart-failure although in January of 1929 he was again referred for hospital care because of a typical angina pectoris   The blood pressure on this admission was 120 systolic and 70 diastolic   There was no edema and the urine was clear   It was felt that hypertensive cardiac disease which had led to congestive heart failure in 1924 had resulted in sufficient coronary artery sclerosis to bring about angina pectoris in 1929

The point for which the case is cited, however, is to indicate how urinary findings may clear when congestive heart-failure is relieved thus removing the suspicion that the kidneys are primarily responsible for the hypertension and edema.

The cardiac hypertrophy and subsequent failure with or without hypertension may have been produced from valvular defect or hyperthyroidism and the same clinical picture results, that is, shortness of breath, edema, and albuminuria and the same designation "cardiorenal" disease applied   The kidneys play a very secondary part in the process, it is entirely a question of cardiac disease as may be proved by the response to

satisfactory treatment   It is apparent that a loose terminology
and loose thinking on this question have resulted in bad thera-
peutics and incorrect prognostications

The last variety of case that may present hypertension and
albuminuria as prominent features of the clinical picture is true
chronic glomerulonephritis   This type is frequently difficult to
differentiate from the form of chronic nephritis which represents
progression from essential hypertension except that it is usually
a disease of younger persons and the clinical picture is dominated
by evidences of kidney dysfunction   It begins frequently in
childhood or youth as an acute nephritis following an infection
such as tonsillitis   The process may heal completely or may
progress directly to chronic nephritis   On the other hand it may
clear and recur following repeated strains or infections and even-
tually manifest itself in early adult life by marked evidence of
renal dysfunction   Hypertension and cardiac hypertrophy are
present   Recurrent slight to moderate edema is common   Urin-
ary changes (albuminuria, casts, and red cells), eye-ground altera-
tions, anemia, and nitrogen retention are prominent   Progressive
renal failure results in a death from uremia   The following case
illustrates very well the course of the disease in a woman sub-
jected to the strain of repeated pregnancies

C P , a white woman, aged thirty, was first seen in Novem-
ber, 1926   She had enjoyed good health up until the birth of the
last baby, almost two years ago   She had not been entirely well
since, complaining of weakness and becoming easily fatigued

Physical examination showed a well-nourished woman with
no evidence of organic disease, although there was a slight sys-
tolic murmur at the apex of the heart   The blood-pressure was
140/90 and the urine contained a trace of albumin and a few
hyaline casts   A diagnosis of focal glomerulonephritis was made
In February, 1927 the tonsils were removed   At this time the
urine still showed a trace of albumin and a few hyaline and
granular casts   Tests of kidney function gave a normal response
and the blood-pressure was within normal limits   After ton-
sillectomy she felt quite well but a short time later she became
pregnant   It was considered unwise to permit the pregnancy to

continue and a therapeutic abortion was done in April 1927 following which she remained well for almost a year

Again she became pregnant   She was seen in February 1928 and complained of nausea vomiting headache, nocturia and swelling of the ankles   Now there seemed to be slight enlargement of the heart to the left and there was marked edema of the ankles   The urine contained a cloud of albumin numerous casts, and occasional red blood cells   There was considerable anemia, the hemoglobin was 44 per cent and the red blood-cells 2,630 000   Renal functional tests indicated moderate impairment and blood pressure varied between 160 and 180 systolic over 100 and 110 diastolic   Eye ground examination was difficult because of an old keratitis but the disk was pale and the arteries were small   Again therapeutic abortion was performed but after discharge from the hospital the patient continued to bleed from the uterus   Convalescence was slow and it was not until April, 1928 that she felt much improved

The patient was admitted to the hospital for the last time in January, 1929   She had been confined to bed for the previous three months   There was marked pallor drowsiness and generalized muscle twitchings   The blood pressure was 185 systolic and 80 diastolic.   There was no edema   The urine contained a cloud of albumin and a few hyaline casts   The hemoglobin was 35 per cent and the red blood cells 2 270 000   The blood urea nitrogen attained the high figure of 215 mg   The patient developed convulsions and died shortly after admission

At postmortem, interest centered chiefly on the kidneys which showed typical chronic glomerulonephritis

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POSTOPERATIVE HEMORRHAGE IN HEMORRHAGIC CONDITIONS PROGNOSIS, PREVENTION, AND CONTROL

Introduction —Persons afflicted with a real hemorrhagic disorder, whether symptomatically manifest or not, form but a very small percentage of the population   Those however who mistakenly allege themselves to be "bleeders" constitute a much larger group   When a patient belonging to either of these classes is faced with some sort of surgical operation, even tooth extraction, the physician in charge must appraise in advance the dangers of postoperative hemorrhage

The fact that many self styled "bleeders" are not really "bleeders" at all, and the additional fact that some true "bleeders" stand various operations without mishap, have altogether conspired to make many physicians careless of their responsibility in this connection   The general practice of referring the whole matter to a single, inadequate, and frequently misperformed laboratory procedure—the coagulation time test—is an illustration in point

Diagnosis —No patient who believes himself or herself to be an "abnormal bleeder" or whose personal or family history implies such an affliction should be operated upon (except in emergency) without careful study   The history of alleged hemorrhagic manifestations both in the individual and the family must be recorded in detail and compared with the natural history of the known types of hemorrhagic diathesis   Of course evidence submitted by the patient may be so obviously apocryphal that one may sometimes dismiss it   Such false evidence

may accrue from the patient's prior experience with postoperative hemorrhage (tonsillectomy, tooth extractions, etc) or post-traumatic hemorrhage, neither of which necessarily proves a true hemorrhagic diathesis Yet one must be cautious in throwing out of court such statements They are sometimes significant

Detailed physical examination is of course the next step—with special attention directed by the history The skin and mucous membranes are searched for ecchymoses, petechiæ, telangiectases, jaundice, and signs of anemia The lymphatic structures, liver, and spleen are investigated by palpation The condition of the peripheral and retinal blood-vessels is determined—as is the blood-pressure Sometimes neurologic examination is indicated If hemophilia is suspected the knee-joints may present vital evidence

A tentative diagnosis may be thus usually established with sufficient exactness to guide the examiner in selecting appropriate laboratory tests by which a "final" diagnosis is made It is beyond the scope of this presentation to discuss the differential diagnosis of hemorrhagic diseases [1] Such diagnosis often depends, at least for ultimate confirmation, on the results of certain hematologic tests These tests are for the most part diagnostically qualitative and prognostically quantitative—when taken together with the other data Hence the methods at our disposal for differential diagnosis of hemorrhagic conditions are at the same time our chief aids in assessing operability (i e , prognosis from the standpoint of postoperative hemorrhage)

Hematologic Methods for Assessing Operability —These methods are first complete blood-count—including "differential" with Wright's stain, reticulocyte count with cresyl-blue stain, and occasionally oxydase stain, second, platelet count, third, coagulation time test, fourth, bleeding time test, fifth, clot retraction test, sixth, tourniquet test, and occasionally, prothrombin time test, van den Bergh test, sedimentation rate (suspension stability) of erythrocytes, blood fibrin determinations and other quantitative blood chemical studies

The technic of these diagnostic and prognostic methods and

their general clinical significance need not be here discussed
Reference will be made however to some of them in connection
with assessing operability in the more important hemorrhagic
disorders

Methods of Prevention and Control—Prevention and control of postoperative hemorrhages in hemorrhagic conditions depend upon the proper selection of cases for elective operations, the type of anesthetic employed the nature and site of the proposed operation, careful local hemostasis in the field of operation, and the employment of measures to combat the specific blood defect   It is with these latter measures that we are chiefly concerned   They include blood transfusion, parenteral protein injections of various kinds, x ray irradiations, glucose infusion (intravenous), calcium and parathyroid therapy, liver diet, high vitamin diets, ultraviolet ray therapy, the use of certain drugs such as morphin, and finally, the operation of splenectomy when specifically indicated   The various "systemic coagulants" on the market for oral administration have, in the writer's experience, failed to prove themselves of value

We shall now discuss briefly the more important individual types of hemorrhagic diathesis in relation to postoperative hemorrhage—correlating and applying to specific examples the chief diagnostic, prognostic, and therapeutic methods previously discussed

Chronic thrombocytopenic purpura (primary) is amenable to "clinical cure" or "near cure" in about 75 per cent of the cases by the operation of splenectomy   Modern statistics indicate that splenectomy in this disease is a remarkably safe procedure   It not only produces no postoperative hemorrhage, but usually stops other "spontaneous" hemorrhages which may be going on at the time

Other operations, such as surgical removal of infected teeth or tonsils, are sometimes advisable   Here the pros and cons must be weighed with great care   Local surgical hemostasis is difficult in these areas and serious hemorrhage may occur No such operations of election should be performed on any case of *active* purpura hemorrhagica   The disease should be first

brought under control by transfusions, massive x-ray irradiation of the spleen,[2] or by splenectomy, or the operator should wait for a spontaneous remission   No patient should be operated on (except by splenectomy or in a vital emergency) whose bleeding time is more than ten minutes or whose platelet count is below 40,000 per cubic millimeter   In such cases, blood transfusion is of tremendous value—though it sometimes must be repeated every two to four days (the probable duration of "life" of the infused blood-platelet substance)   Transfusion of "citrated blood" has proved itself just as effective as "unmodified blood" in the experience of the writer   Additional methods of combating[3] the hemorrhagic diathesis of this disease are parenteral protein injections (whole blood, sterilized milk, "coagulose," horse-serum, etc), ultraviolet-ray therapy and liver diet   None of these is as effective as splenectomy in a well-established chronic, severe case of the disease

Case Report—A young girl (A S) had been treated in the University Hospital Clinics over a period of two years for chronic purpura hemorrhagica by x-ray irradiation of the spleen when, at the age of eighteen, she developed acute appendicitis   She had had no hemorrhagic manifestations for more than a year prior to her appendicitis although her platelet count was constantly around 40,000 per cubic millimeter   On admission to the surgical service with the usual evidences of severe appendicitis her platelet count was only 35,000   Leukocytes numbered 16,000   Bleeding time was three minutes (high normal) and clotting time (venous) was also normal (six minutes) as were hemoglobin and red cell figures   Tourniquet test was negative   Clot retraction was absent   Operation was advised with expectation that no serious postoperative hemorrhage would occur   The bases for this favorable prognosis—in spite of the very low platelet counts—were first, clinical quiescence of the hemorrhagic phenomena, and second, normal bleeding time   Dr Eliason operated under local and gas anesthesia   He removed an acutely inflamed appendix   No abnormal bleeding occurred —either at operation or during convalescence   The donor for blood transfusion, ready for use when necessary, did not have

to be employed   Hematologic tests after operation gave results
identical with those found before

This case illustrates the point that no single test can be
taken by itself as conclusive   It is usually stated that hemor-
rhages occur when platelets fall below 60,000 per cubic milli
meter, but this is not always true   Furthermore, "bleeding
time" prolongation does not *always* parallel thrombocytopenia
Hemorrhages may occur in this disease with a platelet count of
100 000 and no hemorrhages with a platelet count of 20 000

One final point regarding females with chronic purpura
hemorrhagica—menstrual time is a dangerous one for many of
them   Something happens at menstruation which renders them
more liable to hemorrhages

Hemophilia is strictly a disease of males if one accepts the
view of hematologic purists   While admitting the genetic pos
sibility of female hemophiliac bleeders (*i e*, half the daughters
of a hemophiliac father and a "conductor" mother) the critical
student of the subject finds no authentic well studied case
of such on record   The alleged female hemophiliacs reported in
the literature fail to meet modern requirements for this diag
nosis   They belong more probably in other hemorrhagic cate-
gories (*e g*, hereditary hemorrhagic telangiectasia,[4] hereditary
thrombocytopenic purpura, hereditary hemorrhagic thromb
asthenia,[5] hereditary hemoptysis,[6] familial epistaxis,[7] heredi-
tary hematuria, hemorrhagic disease of the newborn, and the
so far unnamed hemorrhagic diatheses described by Griffin,[8]
Mmot,[9] and Buckman [10]   A large number of cases are desig
nated "hemophilia" merely because of postoperative hemor
rhage which could more readily be ascribed to unsuccessful or
faulty ligature at operation

The diagnosis of hemophilia, aside from its sex linked he
reditary features and other fairly characteristic manifestations
(*e g* hemarthrosis), rests on demonstration of prolonged co
agulation time of the blood   The occasional spontaneous, ap-
parently non hereditary case of hemophilia emphasizes the im
portance of the test   This test is frequently employed and is
often misapplied and misperformed   Especially is this true in

so-called routine preoperative study of patients about to undergo tonsillectomy, etc   This indictment of the routine preoperative coagulation-time test is made on two counts   first, the usual method employed and, second, its misapplication

The various methods in which "finger prick" blood is used to test clotting time are fallacious   Such methods may defeat the chief purpose of the test which is to detect hemophilia   It is well known to workers in this field that hemophiliac blood *may* clot within normal limits of time when obtained by finger prick   The admixture of tissue juices is often sufficient to nullify the hemophiliac clotting defect and such blood may be reported as "normal"   The same blood obtained by direct venipuncture and tested by the method of Lee and White may show a marked prolongation of the clotting time   This venous blood method is so simple that there is really no excuse for using "capillary-blood" methods—except sometimes in infants and others in whom venipuncture is difficult or impossible   In the latter instance the limitations of the method must be admitted and recognized in interpreting results

Misapplication of the clotting time test as a preoperative routine is apparent when one considers the fact that few conditions are known to be associated with a material prolongation of coagulation time   Hemophilia is the chief one, a rare disease, and strictly confined to males   A moderate prolongation of clotting time is found in some cases of advanced obstructive jaundice and severe hepatic degenerations, in some cases of marked erythemia, and in some forms of hemorrhagic disease of the newborn   It has been similarly noted occasionally in profound anemias of various types, in aplastic anemia, in malignant cachectic states, and in the terminal uremia of nephritis   Prolonged coagulation time may be induced experimentally by acute anaphylactic shock (*e g ,* Witts Peptone) and occasionally in humans as a result of transfusion from an incompatible donor   The only other condition in which a material prolongation of coagulation time has been noted is that recently described by Buckman [10]   This will be discussed later

Of all these disorders the only ones which need be considered

from the standpoint of *routine* preoperative clotting time tests are hemophilia, hemorrhagic disease of the newborn and Buckman's "disease." Patients afflicted with any of the other above-mentioned conditions will surely not present themselves as candidates for casual or elective surgical operation. As a routine preoperative procedure therefore the coagulation time test is justifiable only in male patients to uncover that rare condition "spontaneous hemophilia" and in infants and children of either sex (together with other appropriate tests) to determine the presence of otherwise occult hemorrhagic disease of newborn or of Buckman's disease. In as much as these two latter conditions are usually symptomatically manifest one need have no serious fears of overlooking a hidden hemorrhagic diathesis in females of any age through failure to perform a "coagulation test."

Hemophiliacs are, above all others, the worst surgical risks from the standpoint of postoperative bleeding. Local hemostatics and blood transfusions are the best available forms of treatment. The only modern advance in the prevention and control of hemophiliac bleeding is the method of Vines,[11] confirmed by Mills[12] of induced anaphylaxis. According to Mills one needs merely to sensitize the patient to sheep or hen serum by a subcutaneous injection of 4 c.c of serum and at the end of seven to ten days to inject a drop or two of the same serum intradermally. The development of a wheal at the site of the intradermal injection indicates successful sensitization and is said to be coincident with cessation of hemophiliac hemorrhagic phenomena and a return to normal of the clotting time lasting several weeks. It is advised that hemophiliacs be retested by intradermal injection every two months to see that they remain "sensitive" so that accidental hemorrhage may be quickly controlled when necessary. If this method is as good as is claimed it ought to be helpful in preparing a hemophiliac patient for some necessary operation.

Leukemic hemorrhages, from the standpoint of surgery, are usually in the form of prolonged bleeding from tooth extraction. A complete blood count usually establishes the diagnosis. The other "coagulation factors" are of minor importance. Tourni

quet test is usually positive, platelets are often reduced in acute leukemia and in chronic lymphatic leukemia, and with this there may be a prolonged bleeding time   Endothelial damage by leukemic infiltration and thrombosis is the basis for most of the hemorrhages in leukemia

A minor surgical operation, such as removal of a gland for biopsy study, is usually well borne by chronic leukemic patients Splenectomy has been performed at the Mayo Clinic[13] in about 40 cases of myelogenous leukemia with less than 5 per cent "hospital mortality "

Roentgen ray therapy is advised as a preoperative routine Judging from the recent report of Strumia[14] however, one should not undertake any sort of operation too soon (i e , within several days) after an x-ray treatment during which period the bleeding time was found to be markedly increased in 2 cases treated by Strumia's method

In **aplastic anemia** which has reached the stage of hemorrhages no operation is without serious danger   Transfusions constitute the only effective method of control, and this often only for a few days at a time

It is in certain cases of chronic anemia on the diagnostic borderland between chronic thrombocytopenic purpura on the one hand and chronic aplastic anemia on the other that the pros and cons of operation (i e , splenectomy) become of vital importance

Case Report —C G , a man of sixty-one, complained of gradually increasing weakness and some epigastric discomfort for ten months prior to admission to Dr Alfred Stengel's service Examination at this time revealed severe anemia, small purpuric lesions of generalized distribution, and moderate edema of the ankles   This patient was studied in the ward for many months and we were unable to arrive at a satisfactory diagnosis   The picture was that of profound and increasing anemia of the "secondary type" with leukopenia and increasing thrombocytopenia At first, there was only occult blood in the stools but later, frank melena occurred and marked oozing of blood from the gums The diagnosis lay between aplastic anemia on the one hand and

chronic thrombocytopenic purpura on the other   Injections of
adrenalin and injections of foreign protein (aolan) failed to pro-
duce any increase in leukocytes or platelets   Blood transfusions
(citrate) controlled the bleeding for a few days at a time   Plate-
lets toward the end ranged from 5000 to 20,000, bleeding time
from four to ten minutes. Clotting time was normal   Tour-
niquet test was always positive   The stained smear of the blood
showed a few reticulocytes, an occasional normoblast, and about
50 per cent neutrophilic leukocytes and 50 per cent lympho-
cytes and monocytes   Of the polymorphonuclear neutrophils
there were always a few young forms and an occasional myelocyte
Bone marrow puncture (sternum) showed a fairly normal picture
of active hematopoiesis   The patient bled from this sternal
puncture for a week   Summing up all the evidence it seemed
proper to view the case as one of primary thrombocytopenic
purpura with beginning (but not complete) secondary aplasia of
hematopoietic organs   On this basis and because all other therapy
(including liver diet, ultraviolet ray, aolan injections, and 8
blood transfusions) had failed, splenectomy was performed
(Dr Eldridge Eliason, 10/17/28)   There was no local post-
operative hemorrhage and a transfusion given just before op-
eration effectively prevented *undue* hemorrhage at the time of
operation   The splenectomy failed, however, to produce any
effect on the blood picture   Little or no leukocytosis occurred
and the platelet count never went above 20,000   Hemorrhages
from the mouth recurred two days postoperatively and con-
tinued till death eight days after operation   Autopsy showed
nothing except the usual effects of profound anemia   The mar-
row of tibias and femurs was entirely fatty but the rib marrow
was literally packed with active hematopoietic tissue—both red
and white   No megakaryocytes could be found (the supposed
progenitors of blood platelets)

In retrospect it would seem that splenectomy might have
been effective had it been performed six months earlier   An-
other point exemplified in this case is that "aplasia" of bone
marrow is a relative condition and that diagnostic marrow
puncture can, at best, give information concerning only one

minute part of the bone-marrow system Such "puncture diagnosis" may be entirely misleading and is not without danger

Pernicious anemia patients stand surgical operations quite well Furthermore, thanks to liver therapy, the management of this disease has been miraculously improved and simplified It is not generally appreciated, however, that hemorrhagic phenomena may be occasionally quite severe in this disease—simulating bleeding peptic ulcer, uterine hemorrhage from fibroids or carcinoma, or even purpura hemorrhagica itself Such hemorrhages in primary pernicious anemia are due to the characteristic thrombocytopenia which may be occasionally quite marked (30,000 to 50,000 platelets) Liver therapy is specific

Hemolytic ictero-anemia, splenic anemia, and **Banti's disease** are, like chronic purpura hemorrhagica, sometimes amenable to cure or "near" cure by splenectomy These are, however, rarely in themselves true hemorrhagic diseases For the most part the hemorrhages that do occur (hematemesis and melena) are the result of mechanical factors—rupture of gastric and esophageal varices As pointed out by Miller[15] the varices of splenic anemia are probably caused by active congestion from arterial obstruction in the spleen rather than by venous engorgement from hepatic obstruction In some of the cases of Banti's disease, according to Rosenthal,[16] there is an additional factor—namely thrombocytopenia These low platelet cases of Banti's disease respond best to splenectomy whereas the high platelet cases are liable to recurrent hematemesis even after splenectomy Rosenthal believes this unfortunate sequence is due to post-splenectomy thrombocythemic crises which cause venous thromboses and thus predispose to massive hemorrhages Miller (loc cit) on the other hand attributes the post splenectomy hematemesis in splenic anemia and Banti's disease to a continuation of the original pathologic process—a shunting of arterial blood under high pressure from the splenic artery into the small gastric vessels It would seem that both of these factors may be operative Certainly one sees an occasional case of Banti's disease with a true hemorrhagic diathesis (purpura, epistaxis, etc) associated with thrombocytopenia The best results of

splenectomy obtain in this type of case and in hemolytic ictero-anemia, in which postoperative hemorrhage is rarely encountered. Miller's suggestion of ligation of the splenic artery proximal to its gastric branches in performing splenectomy in these diseases is worthy of trial.

Prolonged obstructive jaundice carries a surgical hazard of major importance—only a part of which is concerned with postoperative hemorrhage.[17] In assessing operability from the latter standpoint, coagulation time determinations and blood calcium tests are the methods usually advised. The writer has found these of little or no practical value and the same is true of the current practice of preoperative calcium therapy (including parathormone injections) in attempting to prevent hemorrhage. The coagulation time test in obstructive jaundice is *usually* within normal limits—in spite of which a few of these patients do bleed abnormally at operation and afterward. When a really significant prolongation of coagulation time occurs (more than ten minutes by Lee and White method) in obstructive jaundice the patients are usually far gone with advanced hepatic degeneration.

The best pre- and post-operative therapy for patients with obstructive jaundice is glucose intravenously. In addition to furnishing the "fuel of life," glucose is the substance *par excellence* for stimulating hepatic regeneration. Furthermore, Ravdin has demonstrated what appears to be a fairly specific diminution in coagulation time from intravenous injection of glucose.

Ravdin's work is still in progress and his report will be awaited with interest. It would seem that intravenous injections of hypertonic glucose solution will have a wide field of usefulness in the therapy of this and some other forms of hemorrhagic disorder.

Patients with advanced arteriosclerosis and with marked hypertension occasionally die at or shortly after operation from cerebral hemorrhage. In addition, such operations as tooth extraction and tonsillectomy are sometimes followed by postoperative hemorrhage. Assessing operability in such cases is a

problem of general clinical practice rather than of hematology
The tourniquet test may give some information of prognostic
value however   In general, operations in such cases are safest
under local anesthesia or open-drop ether anesthesia   The
"closed" methods of general anesthesia are contraindicated be-
cause of their asphyxial pressor effects   Morphin before and
after operations is usually advisable   We have recently dis-
covered that morphin may increase blood fibrinogen in experi-
mental animals (dogs)   Work is now in progress concerning this
matter

The existence of **atypical hemorrhagic conditions**—especially
in children—should make one always cautious in passing judg-
ment   When confronted with a patient whose personal history
is really suggestive of some "bleeding tendency" no matter how
bizarre it may sound, all available coagulation factors should be
studied   Interesting observations by Minot[9] have established
the existence of a familial hemorrhagic disorder characterized
by prolonged bleeding time without other demonstrable ab-
normality   Similarly Buckman[10] has recently described an
hereditary bleeding tendency characterized by prolongation of
clotting time and differing from hemophilia chiefly in its occur-
rence in both sexes, in absence of sex-linked heredity, in absence
of hemarthrosis, and in the presence of an associated prolonga-
tion of bleeding time with normal platelet count   This also dif-
fers from hemophilia in that platelet function is normal as re-
gards specific correction of clotting defect of a sample of known
hemophiliac blood

Little is known of these conditions   It would seem reason-
able to assume however, that the results of bleeding time and
clotting time tests together with the clinical data should enable
one to assess them fairly accurately from the standpoint of op-
erability   Transfusion seems to be the most useful treatment

An additional reason for diagnostic and prognostic caution
in this field is that some of the hemorrhagic disorders (e g ,
hemophilia and purpura hemorrhagica) are subject to remissions
in which tests of coagulation factors may be misleadingly nor-
mal

Hereditary hemorrhagic telangiectasia is no contraindication to operation. Its hemorrhagic manifestations are not based on any known blood diathesis and local postoperative hemorrhage does not occur. The same may be said of the non thrombocytopenic forms of purpura.

Summary and Conclusions —No single preoperative "test should be relied on to determine operability from the standpoint of postoperative hemorrhage. If any preoperative "routine" of this kind is to be enforced the minimal requirements are (1) coagulation time test (venous blood) (2) bleeding time test, and (3) inspection of stained film for evidences of marked abnormalities in the erythrocytes, leukocytes, and platelets.

To assess operability in known hemorrhagic conditions, the proper employment of appropriate tests may give valuable information. These together with clinical knowledge of the particular disorder in hand, make prognosis fairly accurate.

A brief survey of the more important types of hemorrhagic diathesis is presented together with hematologic methods for determining operability from the standpoint of postoperative hemorrhage and a summary of available methods for the prevention and treatment of such hemorrhage.

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REPORT OF A CASE OF PRIMARY PERNICIOUS ANEMIA WITH MULTIPLE NEURITIS AND SUBACUTE COMBINED SCLEROSIS WITH IMPROVEMENT BY LIVER DIET

CASES of pernicious anemia with posterolateral sclerosis and peripheral neuritis are not uncommon but recovery from the neurologic condition is rare The case herewith presented had a marked multiple neuritis and an early posterolateral sclerosis with improvement of both and for this reason is deemed worthy of report

Subacute combined sclerosis was early described by Kohler Pick, and Westphal Its occurrence in primary pernicious anemia was originally mentioned by Addison in 1855 and later by Lichtheim and Minnich Freed ably discusses the pathologic changes occurring in the central nervous system, and divides the involvement as being in the blood vessels, parenchyma, and interstitial tissue The disease originates around and spreads from the vessels, which show thickening and hyalinization of their walls and also some periarterial changes The vascular lumen may become narrowed and is sometimes occluded by thrombi The parenchymal changes are chiefly in the white substance but both myelin sheaths and nerve fibers degenerate The network changes in the axis cylinders give the cord substance a swiss cheese or honeycombed appearance, the so-called "status spongiosis " The primary anemia and sclerosis are generally thought to be due to the same etiologic agent which would sug

gest a hematogenous borne "toxin," if such it may be called
the light of present knowledge

Bubert reports a case of primary pernicious anemia w:
subacute combined sclerosis, in which improvement occurr
with the Murphy-Minot diet

Hassin found in his necropsies of 2 cases of subacute co:
bined degeneration, regressive changes in the nerve-fibers a
progressive ones in the glia   He states that the pathology w
confined to the tracts of Goll and Burdach, the spinocerebell
and crossed pyramidal fibers

As Woltmann states, subacute degeneration is not alo
caused by primary pernicious anemia, but may be due to ma:
other factors and the history should be thoroughly analyze
Some of the additional causative offenders may be the seconda
anemias, leukemias, Addison's disease, pellagra, tuberculos
syphilis, leprosy, malaria, typhoid, alcoholism, diphtheria, lea
arsenic, and phosphorous poisoning and septicemia   With tl
multitude of etiologic contributors pernicious anemia wou
appear a minor agent   Woltmann, however, reports that of 2
unquestioned and not otherwise complicated cases of pernicio
anemia seen at the Mayo Clinic since 1916, 150 were subject
to a detailed neurologic examination of which no less than 8C
per cent presented indisputable evidence of the destruction
nervous parenchyma   This was borne out by von Voss and Mi
nick, who found that pernicious anemia was responsible
one-third of the cases of combined sclerosis   Woltmann furth
states that 12 7 per cent of the patients with pernicious anem
came to the Mayo Clinic because of symptoms specifically d
noting nervous system involvement   Multiple neuritis w
demonstrated in 4 9 per cent of the cases   The cardinal neur
logic symptom is paresthesia   The chief findings upon e
amination are the disturbances of deep sensation such as v
bratory and joint sensibility, and impaired or absent patell
and achilles reflexes   The Babinski sign may often be presen
rarely a transient hemiplegia may occur

Case Report —Mrs J S , white, aged sixty-five, was a
mitted to the University of Pennsylvania Hospital on Januai

11, 1928 with the chief complaints of weakness and inability to walk. These symptoms had developed progressively one month prior to admission. Her past medical history was negative except for a stroke alleged to have occurred four years before, constituting a slight paralysis of the left side of the face only. On examination she was found to have a blood pressure of 136 systolic and 60 diastolic, the characteristic lemon tinge to the skin, a sore tongue, exaggerated reflexes, spasticity of arms, spastic extension of the toes, especially of the right foot, Babinski of the left foot and impairment of vibratory sensation. The blood picture presented a hemoglobin of 27 per cent, red blood cells 980,000, white blood cells 5400, polymorphonuclears 60, small lymphocytes 33 and large lymphocytes 7, with color index one plus. Nucleated red cells 2 per cent. Fractional gastric analysis showed free hydrochloric acid absent in all specimens and the highest degree of total acidity to be 16. She was given two blood transfusions of 500 c.c. each on September 11th and 15th respectively, and placed on Valentine's liver extract, and a liver diet. On November 19th, 1928 she was discharged from the University Hospital with improvement of her general condition and blood picture, but she remained unable to walk. On November 26, 1928 her family physician, Dr. H. K. Carey, referred her to the Samaritan Hospital, where she was put on Lilly's No. 343 liver extract and a liver diet. The blood-count on admission was as follows: hemoglobin 68 per cent, red blood cells 3,340,000, white blood cells 6000, polymorphonuclears 36 per cent, large lymphocytes 34 per cent, small lymphocytes 28 per cent, and eosinophils 2 per cent. Nucleated red cells 1 per cent. There was marked anisocytosis, poikilocytosis, and polychromatophilia.

The physical examination showed hyperexcitability of reflexes of lower extremities, Babinski of left side, inability to stand or walk, impairment of vibratory sensation of lower extremities, no bladder or bowel disturbances, pain and temperature sensibility preserved. At no time during her stay in the hospital were there more than 1 per cent nucleated red cells nor did the blood count improve to any extent as compared with that upon

admission   After two months, however, she regained the ability to stand and walk to such a degree that she required no aid   On January 30 1929, she was discharged as markedly improved in her general condition, and well able to walk with no sign of ataxia whatever

A recent follow-up examination at home, where social conditions are very poor, reveals the red blood-cells to have dropped to 2,940,000, hemoglobin 60 per cent, polymorphonuclears 50 per cent, small lymphocytes 35 per cent, large lymphocytes 3 per cent   eosinophils 7 per cent, transitionals 4 per cent, mononuclears 1 per cent   She carries on a considerable portion of her housework and her locomotion is excellent   As regards personal care, gross negligence exists   Sometimes the liver is eaten but more often it is not   Her mentality is good except that she displays a delayed reaction and peculiar hesitant and confused manner in obeying commands   Her station and gait are normal, vibratory sensation is still somewhat impaired in lower extremities, joint sensibility is normal, superficial discrimination, and temperature and pain sensation are normal   Babinski persists in left foot and there is slight spasticity of both lower extremities   Due to the type of patient and poor co-operation no gastric analysis could be obtained at the Samaritan Hospital, and also for this reason her case cannot be as closely followed at the present time as we would like

Summary —A case of primary pernicious anemia with multiple neuritis and subacute combined sclerosis presenting all the signs and symptoms of this disease, corroborated in diagnosis both at the University Hospital and Samaritan Hospital   When admitted to the latter institution, this patient could neither stand nor walk, but rapidly improved under routine liver therapy, until upon discharge she was well able to navigate unaided, and carry on the minor duties of her household   This case is reported because improvement in the neurologic involvement in primary pernicious anemia is rarely seen

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A COMPARATIVE CLINICAL AND ROENTGEN STUDY OF THE HEART BORDERS

SINCE the accuracy of the percussion measurements of the heart is questioned by many eminent authorities,[1] a comparative study with teleoroentgenographic measurements as control was made in a series of 200 cases It is only by such a comparative study that the true value of clinical percussion can be determined Two hundred cases of both sexes and all ages from eleven to seventy-six years were included since a mean was sought utilizing a cross section of clinical material It was realized that a careful and uniform technic must be used by both clinician and roentgenologist in order to make comparative study and we therefore adopted the following technic for routine use [5] [6]

Clinical Measurements —The patient is examined in a standing position, arms falling naturally and easily beside the chest to take advantage of the more marked cardiac impulse in the erect position, from which it naturally follows that the sensation of resistance under the finger during percussion is more appreciated The erect position is used for the following reasons The cardiac impulse is generally less marked in recumbency, and can often be felt *only* when the individual is erect, the heart being further from the anterior chest wall in the recumbent position The sensation of resistance under the finger during percussion is as helpful as the change of note to the ear In the sitting position, especially if sitting in bed, the heart may be displaced outward and upward to an appreciable degree due to pressure of the diaphragm, meteorism, ascites, pregnancy, etc.

A moderately light percussion stroke is used in determining the left border of cardiac dulness, while a slightly heavier percussion stroke is used on the right side

To determine the so-called "mid-clavicular line," the clavicle is measured from the middle of the suprasternal notch to a perpendicular line dropped from the outer end of the clavicle Half this measurement is taken as the mid-clavicular line The outer end of the clavicle is found by running the finger along the superior surface of the clavicle, rather than the anterior border, the external end being recognized by the depression between the outer end of the clavicle and the acromium process of the scapula

The lowermost, outermost point of the apical impulse is determined by inspection and palpation, and the location is noted

Fig 165 —The cardiac borders

in centimeters both from the mid-sternal line and the mid-clavicular line All measurments are recorded to the nearest 0 5 centimeter

The middle finger of the left hand is then pressed firmly against the chest wall in the fifth intercostal space parallel with and between the ribs Percussion is started from just outside the apical impulse and carried toward the heart and note made of the point at which clear pulmonary resonance is definitely impaired The record from this point to the mid-sternal line is taken as the median left measurement

The median right measurement or the right border of cardiac dulness is obtained by percussion from just inside the right mid-

clavicular line toward the heart in the fourth intercostal space
The sum of these two measurements, that is, the median right
and the median left is used as the total cardiac width or trans
verse diameter of the heart

In determining the thoracic measurment, a tongue depressor
is placed against the lateral chest wall at the level of the fifth
interspace in a sagittal plane   The measurement is noted from
the inner side of the tongue blade to the mid sternal line and

TABLE I

MEDIAN RIGHT MEASUREMENTS

CLINICAL	ROENTGEN	VARIATION
4 5 cm	5 5 cm	-1 0
4	4 5	0 5
4	4 2	-0 2
4	3 8	+0 ?
4	4 5	-0 5
4 5	5 7	-1 2
4	4 2	-0 2
4 0	5 2	-1 7
4	6 1	-2 1
4	4 3	-0 3
3 5	4 5	-1 0
5	4 8	+0 ?
4 5	4 1	-0 1
4	4 2	+0 3
4	4 2	-0 2
4 5	4 5	0 0
3 5	4 6	-1 1
5	7 1	-2 1
4 5	4 8	-0 3
4 5	4 3	+0 2
5	5	0 0
5	5 5	-0 5
4	4 2	-0 2
6	6 4	-0 4
3 5	5 2	-1 7
5 0	5 6	-0 6
3 5	4 3	-0 8
4	4 6	-0 8

multiplied by two   Making the measurement with a pelvimeter
at the same points, it was found that the method described above
was accurate, with an average error of less than 0 5 centimeter
and since it required no special instrument, this procedure was
used in making the thoracic measurements

The supracardiac dulness in all cases is measured in the first
and second interspace

A moderately light percussion stroke is used in determining the left border of cardiac dulness, while a slightly heavier percussion stroke is used on the right side

To determine the so-called "mid-clavicular line," the clavicle is measured from the middle of the suprasternal notch to a perpendicular line dropped from the outer end of the clavicle Half this measurement is taken as the mid-clavicular line   The outer end of the clavicle is found by running the finger along the superior surface of the clavicle, rather than the anterior border, the external end being recognized by the depression between the outer end of the clavicle and the acromium process of the scapula

The lowermost, outermost point of the apical impulse is determined by inspection and palpation, and the location is noted

Fig 165 —The cardiac borders

in centimeters both from the mid-sternal line and the mid-clavicular line   All measurments are recorded to the nearest 0 5 centimeter

The middle finger of the left hand is then pressed firmly against the chest wall in the fifth intercostal space parallel with and between the ribs   Percussion is started from just outside the apical impulse and carried toward the heart and note made of the point at which clear pulmonary resonance is definitely impaired   The record from this point to the mid-sternal line is taken as the median left measurement

The median right measurement or the right border of cardiac dulness is obtained by percussion from just inside the right mid-

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CLINICAL	ROENTGEN	VARIATION
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4	4 5	0 5
4	4 2	-0 2
4	3 8	+0
4	4 5	-0 5
4 5	5 7	-1 2
4	4 2	-0 2
4 0	5 ?	-1 7
4	6 1	-2 1
4	4 3	-0 3
3 5	4 5	-1 0
5	4 8	+0 2
4	4 1	-0 1
4 5	4 ?	+0 3
4	4 2	-0 2
4 5	4 5	0 0
3 5	4 6	-1 1
5	7 1	-2 1
4 5	4 8	-0 3
4 5	4 3	+0 2
5	5	0 0
5	5 5	-0 5
4	4 2	-0 2
5	5 4	-0 4
3 5	5 2	-1 7
5 0	5 8	-0 8
3 5	4 3	-0 8
4	4 8	-0 8

multiplied by two   Making the measurement with a pelvimeter
at the same points, it was found that the method described above
was accurate, with an average error of less than 0.5 centimeter
and since it required no special instrument, this procedure was
used in making the thoracic measurements

The supracardiac dulness in all cases is measured in the first
and second interspace

Roentgen technic

Fluoroscopy is always made the first part of the examination for the following reasons   Any undue effect on the size and shape of the heart caused by respiration, posture of the patient or pulmonary pathology can often only be obtained by the fluoroscopic examination   It often supplements physical examination for analysis of the relative type of chest and heart that is being examined   Deformities of the chest, especially spinal deformities, can be quickly seen   The relative position of the heart and diaphragmatic cupolæ is noted so that the central Roentgen ray during the teleoroentgenographic examination can be directed at the proper level   Additional information gathered from the oblique and lateral positions is also made available

One of the most frequently encountered problems during a teleo-examination is the control of the patient's respiration   Observation of the way the patient regulates his breathing in accordance with the roentgenologist's instructions is best done during the fluoroscopic examination and correction made and checked immediately   It is surprising how few patients comply with directions the first time   Practice is usually necessary before the average patient manages to cease respiration completely, at the desired phase of the respiratory cycle

The roentgenographic examinations are made with the patient in the erect position   The hands are allowed to hang loosely by the side, and the shoulders are allowed to fall forward till the tips of the acromium processes touch the casette   Undue elevation of the shoulders is to be guarded against and this is aided by allowing the hands to hang loosely by the side   If the hands are placed on the hips, there usually follows an unnatural elevation of the shoulders which has an appreciable effect on the location of the mid-clavicular line   Furthermore, this position is at variance with that assumed by the patient during the clinical examination and thus errors arise that preclude comparison   A film target distance of two meters is used consistently   The central ray is usually directed in the sagittal plane on the level of the sixth dorsal vertebra, but this often varies depending on the fluoroscopic findings   If the heart is of the long dropped or

pendulum variety, or if the domes are arched relatively high on each side as is sometimes seen in sthenic and fat individuals, the seventh and rarely the eighth dorsal vertebra is chosen. The exposure time is the fastest practical time interval possible and this ranges from one-thirtieth to one tenth second with our equipment. (We did a short series of cases using one-one hundred and twentieth second exposure time, but we markedly shortened the life of our Coolidge tubes and so we discontinued this technic.) Duplitized films are used. Great care is always exercised to avoid rotation of the patient, and a fixation muslin band across the chest is always employed. The exposure is made at complete respiratory rest just at the end of a normal inspiration, the patient having been previously instructed and trained, if necessary, in the fluoroscopic room not to breathe in too deeply or rapidly and to hold his breath, just as he has completed the normal, natural inspiratory phase.

Measurements on the roentgen films are routinely made as follows (see Fig 166)

The mid-sternal line is drawn vertically midway between the sternal ends of the clavicle. A line is next drawn vertically through the extreme lateral end of the left clavicle. The line A–B is then drawn through the long axis at the clavicle, and where this line intersects the mid sternal line, a fourth line is drawn horizontally to the left axilla (line A–C, see Fig 166). The clavicular angle is thus formed by the lines A–B and A–C and furnishes us an accurate means of determining the amount of inward shift of the mid-clavicular line.

The other measurements of the heart routinely noted are the aortic width in the first interspace, the width in the second interspace, the median right width in the fourth interspace, and the median left width in the fifth interspace. The greatest median right and median left measurements often did not correspond with these interspaces, but for this analysis, the variation was disregarded since the clinical measurements were made in these interspaces and analogous measurements for comparison are necessary.

In 87 per cent of the cases of our series, the mid spinal line

was slightly to the right of the mid-sternal line even though we exercised great care in avoiding rotation of the patient during the examination   The frequency of this finding made us suspect that this is probably a normal finding in right handed individuals Since the clinical measurements were made from the mid-sternal line, we also adopted this line in order to obtain measurements that could be used for comparison

The average clavicular angle (that angle formed by lines A–B and A–C) was 14 degrees, varying through an arc of 41 degrees Placing the hands on the hips almost always increases this

Fig 166 —Cardiac measurements and clavicular angle—C–A–B

angle   Since the mid-clavicular line is placed on a horizontal line midway between the mid-sternal and the vertical line dropped from the lateral end of the clavicle, the greater the obliquity of the clavicle, the nearer to the mid-sternal line moves the mid-clavicular line   If this angle is considerably increased or if the length of the clavicles is unduly great, this shift may amount to 10 per cent and may mean as much as 2 cm difference in the location of the mid-clavicular line   Therefore, these factors must always be carefully considered if the size of the heart is to be determined by the comparative locations of the left cardiac border and the mid-clavicular line

Results —Table I is a partial list of the median right meas
urements as recorded both from clinical and teleroentgenographic
examination It demonstrates clearly how the tendency of the
clinician is to underestimate this measurement [4] In 76 per cent
clinical were less than the Roentgen measurements while in only
18 per cent were they more

The greatest clinical variation was an underestimation of 2 1
cm from the true Roentgen margin The average variation was
an underestimation of 0 5 cm In other words, the percussion
margin is likely to be underestimated in about 5 cases out of
every 7, averaging only 0 5 cm The greatest amount of varia-
tion of clinical underestimation occurred in cases of mitral
stenosis, emphysema, kyphosis, sthenic, and obese individuals
in the order named

TABLE II
MEDIAN LEFT MEASUREMENTS

CLINICAL	ROENTGENOLOGIC	VARIATION
11 cm	10 5 cm	+0 5 cm
10 7	10 5	+0 2
8	8 7	-0 7
10	9 6	+0 4
11	11 1	-0 1
10	9	+1 0
10	11 8	-1 8
9	8 7	+0 3
14 8	12 2	+2 4
9	9 2	-0 2
8	6 2	+1 8
8 5	7 6	+0 9
10	10	0 0
11	10 5	+0 5
13	11	+2 0
9	8 9	+0 1
9	8 6	+0 4
14	12	+2 0
11	9 2	+1 8
11	10 1	+0 9
12	11	+1 0
10	10	0 0
7	7 1	-0 1
14	13 5	+0 5
14	12 5	+1 5
9	8.5	+0 8
9 5	8 5	+1 0
11	10 6	+0 4

Table II is a comparison of the clinical and Roentgen median
left measurements namely, the distance of the left border from

the median line in the fifth interspace   In 72 per cent the clinical
measurement was greater than the Roentgen dimension and it is
relatively greater, the greater the left ventricular enlargement
Thus, in cases of aortic regurgitation, the clinician overestimates
this margin most, while in mitral stenosis, he approximates the
Roentgen determination more closely   In this series, the clinical
median left border was less than the Roentgen border in only 19
per cent , and these were mostly in cases of asthma and em-
physema   Figure 167[3] shows how the difference in the relative
shape of the heart to the anterior chest wall accounts for this
phenomenon   The average clinical variation was only 0 4 cm

R–R$_r$—Roentgen projections
P–P$_1$ —Percussion measurements
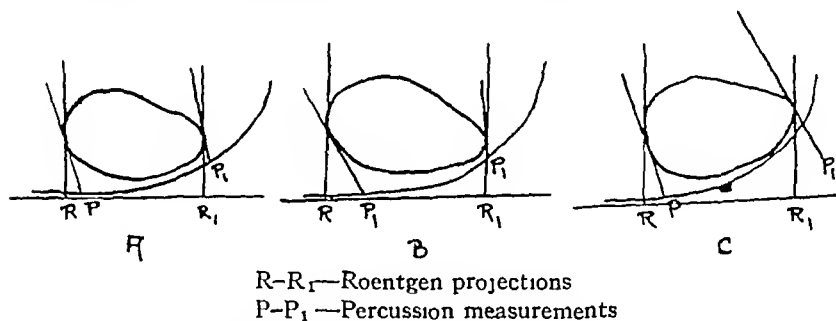
Fig 167 —A, Normal heart—clinical and roentgen measurements prac-
tically similar excepting that clinical M R is less and M L is more than the
Roentgen measurements
        B, Mitral stenosis   Clinical M R is relatively more underestimated
than Roentgen M R lengths
        C, Aortic regurgitation   Clinical M L is relatively more overestimated
than Roentgen M L

overestimation and the greatest increase of the clinical left mar-
gin to the left of the Roentgen margin was 2 4 cm   Thus, the
clinician tends to overestimate this border in about 5 cases out
of 7, but with only an average overestimation of 0 4 cm
    Table III is a comparison of the clinical and Roentgen tho-
racic measurements   This comparison must necessarily con-
sider the factors of Roentgen aberrations, and also the differences
in the way the clinical and Roentgen measurements had to be
made   The roentgenologist measures the transverse distance
from the pleural surface of the ribs on a level of the fifth inter-
space while the clinician measured from the skin surfaces on the

same level Ordinarily, this should always make the clinical greater than the Roentgen measurements but the Roentgen factors of aberration compensated for this discrepancy so that in 56 per cent , the clinical were less than the Roentgen diameters and greater in only 39 per cent   The average variation was a decrease in the clinical diameter of 0 18 cm as compared with the Roentgen diameter, but the variations were rather marked

TABLE III
THORACIC MEASUREMENTS

CLINICAL	ROENTGEN	VARIATION
26	27	-1 0
28	30	-2 0
21	23 2	-2 2
28	28 6	-0 6
27	27 2	-0 2
28	31 6	-3 6
28	26 7	+1 3
28	26	+2 0
20	31 5	-3 5
26	26	0 0
24	22 9	+1 1
23	24 5	+1 5
28	29 3	+1 3
23	28 8	-0 8
25	25 6	-0 6
26	26 5	-0 5
22	24	-2 0
27	26 2	+0 8
30	29 1	+0 9
28	28	0 0
32	31 2	+0 8
34	29	+5 0
28	30 2	-2 2
18	18	0 0
28	30	-2 0
26	25 2	+0 8
28	28	0 0
26	24 2	+1 8
24	26 5	-2 5

being overestimated as much as 5 cm or 16 per cent in one case and underestimated 3 6 cm or 17 per cent in another case This comparison shows a great variation in this measurement and this is natural when one considers all the causative factors. Obesity and emphysema were the chief causes for the greatest discrepancies, producing very variable clinical measurements and marked Roentgen aberrations

Table IV shows the comparative clinical and Roentgen transverse measurements between perpendicular lines dropped from the lateral ends of the clavicles   The clinical averaged 0 05 cm greater than the Roentgen measurements   This close approximation is natural since this measurement is easily determined by both the clinician and roentgenologist and no factors of variation due to pathologic changes enter into the examination There is no appreciable Roentgen aberration because the ends of the clavicles are placed very close to the film   The greatest increase of the clinical over the Roentgen measurement was only 4 cm or 9 per cent in 1 case and the greatest decrease was 3 4 cm or 8 per cent at the other extreme

TABLE IV

CLAVICULAR MEASUREMENTS

CLINICAL	ROENTGEN	VARIATIONS
32 cm.	31 cm	+1.0 cm
36	34	+2 0
28	30	−2.0
36	35	+1.0
32	31	+1.0
36	36.8	−0 8
32	35.2	+0.8
32	30.6	+1.4
32	32	+0.0
30	29.2	+0.8
32	32.4	−0.4
28	31.2	−3.2
38	36 8	−0.8
32	30.8	+1.2
36	32	+4.0
32	33.2	−1.2
30	32 8	−2.8
30	33.2	−3.2
36	32.4	+3 6
32	33	−1.0
36	34	+2 0
34	34.4	−0.4
20	20.4	−0 4
36	35 6	+0.4
34	35 2	−1 2
32	32.4	−0.4

The analysis of Table V and Table VI shows that although there is a closer approximation of the clinical with the Roentgen clavicular determinations which would therefore eliminate a variable factor in the cardioclavicular measurements, the clinical

approximations were not appreciably better using such a ratio
The clinical cardiothoracic measurements were as accurate as
the clinical cardioclavicular measurements   The average varia
tion of the clinical cardiothoracic measurements was 0 4 per
cent , while the clinical cardioclavicular average variation was

TABLE V
CARDIO THORACIC MEASUREMENTS

CLINICAL	ROENTGEN	VARIATION
60%	57%	+3%
46%	50%	-4%
57%	56%	+1%
50%	47%	+3%
55%	57%	-2%
51%	47%	+4%
50%	60%	-10%
50%	46%	+4%
40%	49%	-1%
50%	59%	-9%
50%	46%	+4%
52%	50%	+2%
53%	51%	+2%
53%	51%	+2%
66%	59%	+7%
50%	50%	0
60%	53%	+7%
46%	60%	-14%
63%	65%	+2%
55%	50%	+5%
48%	46%	+2%
50%	55%	-5%
53%	51%	+2%
61%	61%	0
71%	65%	+5%
67%	70%	-3%
50%	50%	0
50%	49%	+1%
62%	58%	+4%

0 6 per cent , but the amount of over or under estimation by the
clinical cardiothoracic measurements was slightly greater than
the cardioclavicular measurements

The measurements of the base of the heart are not included in
this report because a separate analysis was made by a different
method of comparison

Summary —1 The clinical measurements of the right heart
border can be made with a reliable degree of accuracy, the ten
dency being to underestimate this margin in about 75 per cent

with the average variation from the normal of only 0 5 cm but
with a possible error of 2 cm in either direction

2 Clinical left border is also accurately determined by clinical
percussion with an average variation of only approximately 0 4
cm , but with a possible over or under estimation of 2 cm   In
75 per cent of the cases there will be overestimation of this

TABLE VI

CARDIO CLAVICULAR MEASUREMENTS

CLINICAL	ROENTGEN	VARIATION
48 %	52 %	-4.0 %
36	44	-8.0
42	43	-1 0
38	38	0.0
47	50	-3.0
40	39	+1.0
43	45	-2.0
43	39	+4.0
42	45	-3.0
43	52	-9.0
37	33	+4.0
43	39	+4.0
41	40	+1.0
46	47	-1.0
46	47	-1.0
40	40	0.0
45	39	+6.0
37	48	-11.0
52	60	+8.0
48	43	+5.0
47	47	0.0
44	45	-1.0
55	55	0.0
55	56	-1.0
41	41	0.0
47	47	0.0

margin, and this tendency increases relatively in those cases
with left ventricular enlargement

3 Cardiothoracic ratio is efficiently determined clinically
with an average variation of less than 1 per cent , but with ex-
treme variations of as much as 10 per cent   The use of the cardio-
clavicular ratio did not reduce this variation appreciably

4 The importance of careful clinical and Roentgen technic,
the cause for variant results, and the necessity for adoption of
uniform procedure of percussion are detailed   With careful at-
tention to this technic, the clinical heart borders, either right or

left can be percussed with an average variation of only 0 5 cm from the teleoroentgenographic heart borders

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CLINIC OF DRS EDWARD STEINFIELD AND HARRY SHAY

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GASTRIC CARCINOMA COMPLICATED BY THROMBO-CYTOPENIC PURPURA

THE co-existence of gastric carcinoma and thrombocytopenic purpura presents an interesting and in some respects a perplexing problem   That these difficulties are not entirely disposed of by necropsy evidence is well illustrated in the following case history

The patient is a married Jewish woman fifty five years of age, her family history reveals no special tendency to blood dyscrasias malignancy cardiovascular disease nephritis or tuberculosis   She has six children two boys and four girls   The oldest daughter has a moderate secondary anemia   About four years before admission, she began to notice abdominal pain localized in the region of the umbilicus   The pain is of a dull character and comes on in paroxysms but has not gotten worse   About four months ago she began to have a sticking pain in the epigastrium two hours after eating   There was also abdominal pain which radiated posteriorly as far down as the lumbar region of the spine   She has vomited food on several occasions, but no blood.   On the morning of admission she became nauseated, vomited a large quantity of blood   and felt herself becoming weaker

Examination on admission (December 13   1927) revealed a middle-aged woman of fair nutrition, but with marked pallor   Profound weakness precluded thorough examination at this time   Subsequent observations indicated no abnormalities of the central nervous system or of endocrine structures   no mouth lesions   and no pulmonary signs   The heart was slightly enlarged to the left and a soft systolic murmur was heard at the

base but not transmitted   Blood-pressure 75/50 to 95/65 during the first week of admission, later readings were as high as 115/75   On abdominal examination, diastasis of the recti was noted, the liver was enlarged 5 cm below the costal margin in the midaxillary line, the spleen was not palpable   An indefinite tenderness was present in the right upper quadrant but no masses were palpated   No purpuric spots were noted on admission   The day after admission the patient vomited a large quantity of fresh blood and gross blood was passed by bowel   She was given hypodermoclysis of 500 c c of saline solution on two successive days and appeared definitely better on December 19th   Bleeding apparently subsided and about two weeks after admission it was considered safe to take roentgenograms of the gastro-intestinal tract   She was still, however, too weak to have satisfactory exposures made   Under these circumstances a report of negative findings was made, though judgment was suspended until the possibility of more thorough x-ray investigation later   During this time the presence of a gastric lesion, either ulcer or malignancy, appeared to be the most likely cause of the bleeding   However, when purpuric spots and ecchymotic areas appeared on the body about three weeks after admission, attention was directed toward the consideration of hemorrhagic purpura   This supposition appeared definitely verified when the hematologic evidence ordinarily associated with thrombocytopenic purpura, was obtained   Various therapeutic measures were used   Calves' liver was used in the diet, liver extract was administered, foreign protein in the form of milk injections was given a trial   Intramuscular injections of blood and four small blood transfusions were given by Dr N Rothschild   As a last resort, x-ray exposure of the splenic area was attempted   None of these measures was of avail in halting the progressive fall in the blood-platelets   Splenectomy was of course considered, but at no time did her condition justify operative risk   There was intermittent loss of blood as evidenced by strong reactions for occult blood in the stools   The platelet count sank to 4000 per cubic millimeter on February 8th and death occurred on February 11, 1928

Laboratory Examinations —Kolmer complement-fixation test for syphilis, negative, Kahn reaction, negative On December 13, 1927, blood urea nitrogen 40 mg, blood-sugar, 150 mg, uric acid, 2 8 mg, creatinin, 1 3 mg per 100 c c of blood On January 23, 1928, the blood urea nitrogen was 16 mg and the plasma CO_2 was 40 volumes per cent Blood-culture, negative Van den Bergh Faint delayed direct indirect, 2 units Bleeding time on January 9, 1928 was eight minutes, coagulation time ten minutes by vein, no clot retraction in twenty four hours, tourniquet test, positive On January 27, 1928, the bleeding time was twenty minutes plus Fragility test Hemolysis began at 0 40 per cent and was complete at 0 32 per cent

Urine Specific gravity varied from 1 010 to 1 022, a faint trace of albumin, no sugar, a few granular casts, a few leukocytes

Feces Occult blood strongly positive during early and latter part of illness

Blood counts are given in tabular form on page 926 to better illustrate the course of the disease

The summary of pathologic findings at necropsy was given by Dr Case as follows

Anatomic diagnosis (1) anemia, (2) fatty degeneration of heart, (3) edema of lungs, (4) cloudy swelling of kidneys (5) cloudy swelling of liver, (6) hemangiomas of liver, (7) single (metabolic) gall-stone, (8) healed gastric ulcer, (9) hyperplastic bone marrow of tibia

Histologic diagnosis Heart myocardial degeneration, fatty degeneration

Lungs Congestion and edema.

Bronchial lymph node Anthracosis

Spleen Excessive amount of hemosiderosis with many large cells—reticulo-endothelial cells

Adrenals The brown nodules seen in the medulla, grossly, proved to be nodules of cortical tissue with brown granules in the cytoplasm

Kidneys Parenchymatous degeneration with foci of chronic fibrosis and cellular infiltration

Stomach The lesion that grossly suggested healed ulcer is

an adenocarcinoma and the mucosa over it is destroyed   Enlarged retroperitoneal lymph-nodes   Secondary carcinoma

Liver   The dark red lesions on the surface are hemangiomas The liver cells show parenchymatous degeneration and the capillaries contain large cells

Gall-bladder   Chronic cholecystitis

Bone-marrow of tibia   There is some hyperplasia but it is not marked   It does not resemble that seen in pernicious anemia

TABLE I

Date 1927	R B C	Hb per cent	W B C	Platelets	Remarks
Dec 13	3,500,000	60	7,200		
Dec 14	3,800,000	50	10,200		
Dec 16	2,160,000	45	10,050		
Dec 17	990,000	28	9,900		
Dec 19	880,000	20	7,750		
Dec 23	1,610,000	27	5,950		2 Myelocytes, marked aniso cytosis, poikilocytosis, polychromasia
Dec 27	1,800,000	38	7,800		
Dec 30	2,200,000		6,950		
1928					
Jan 3	3,470,000		4,600		
Jan 9	2,010,000	28	6,300	66,000	No clot retraction in twenty four hours
Jan 10	2,040,000		8,200	54,000	Polymorphs 58 per cent, old metamyelocytes 10 per cent, young metamyelocytes 9 per cent
Jan 13	1,510,000	21	5,600	41,000	53 Nucleated red cells 6 myelocytes
Jan 14	1,400,000	23	5,300	39,000	Reticulated red cells 21 per cent
Jan 18	1,360,000	27	7,600	40,000	9 nucleated red cells 6 myelocytes
Jan 20	1,520,000	27	9,400	22,000	
Jan 27	1,020,000	18	9,300	13,000	
Feb 2	1,160,000	19	10,100	12,000	Old metamyelocytes 21 per cent, young metamyelocytes 14 per cent, 18 myelocytes, 41 nucleated red cells
Feb 8	890,000	11	14,900	4,000	

Discussion —The appearance of purpuric spots and subcutaneous ecchymoses in conjunction with the hematologic evidence of thrombocytopenic purpura, particularly low platelet counts, prolonged bleeding time absence of clot retraction and normal coagulation time, all seemed to make the diagnosis fairly conclusive The fall in blood platelets was selective since they were depressed out of proportion to the other constituents of the blood-count In addition they were probably functionally changed both in adhesive and retractive quality, if the bleeding time and clot retraction can be taken as criteria of these functions The preservation of one or both of these properties, even when the total number is lessened, explains instances of low platelet counts not accompanied with bleeding It can be estimated that the mechanism of platelet production was selectively depressed in this patient as in many individuals with purpura, because the bone-marrow was still actively producing young red cells and immature leukocytes

The history of abdominal pain in the past was considered to be due to some other underlying condition, inasmuch as it was not accompanied by hemorrhagic manifestations Also, a definite statement of relation to meals was given by the patient It must be said, however, that these points were of more significance in retrospect than in prospect During the time that purpura seemed to be the outstanding feature of the case, the question arose as to the advisability of splenectomy Several points indicated the possibility that this patient might not respond favorably to splenectomy (1) Absence of definite signs of enlargement of spleen, (2) lack of response to foreign protein therapy, (3) the acute course In regard to the first point, in patients of this type, the dysfunction is widespread in the reticulo-endothelial system and removal of the spleen only takes care of one area, important though it may be Despite this theoretical objection Giffin and Holloway[1] have cited the clinical histories of patients in whom removal of a spleen of moderate size has produced a favorable effect upon the hematologic and clinical manifestations of purpura Patients who show some encouraging response to foreign protein therapy appear to possess a re-

serve of recuperative power which enables them to form plate
lets and are apt to show improvement after splenectomy   It is
likely that this possibility is of more importance where dimin
ished production of platelets is the predominant mechanism
The third point is amply confirmed by practical experience
Acute types are not apt to be helped by splenectomy   The
spontaneous downhill course of these patients and the operative
mortality cast grave doubts upon a decision for surgical inter
vention   It is appropriate to again mention the fact there that
none of these theoretical contingencies would have outweighed
the decision for splenectomy, were the patient even remotely
considered safe for this procedure

Other causes of hemorrhage more or less pertinent to the case
in question were under discussion   Among these is an allied
condition styled by Glanzmann[2] "chronic thrombasthenic pur-
pura "   This is a hereditary disease found in both sexes and in
which increased bleeding and coagulation time may be present
The platelets though not greatly reduced are apparently altered
in morphologic and functional characteristics   There is no
particular resemblance to this syndrome in the case under dis-
cussion

Thrombocytopenia, purpura, and hemorrhage are commonly
noted in aplastic anemia   The blood-picture here does not fit
in with this possibility   Large numbers of immature red cells
such as normoblasts, reticulocytes, and cells showing poly-
chromasia, indicated that erythrocyte production was not want-
ing   Granulocytes were also actively produced, and immature
forms were also increased   Particularly was this true of young
metamyelocytes (so-called) ordinarily not present in the nor
mal blood or in the absence of infection   The presence of such
cells are held by some, notably Schilling, to indicate a warning
of the inability of the body to cope with the disease process
The signs of blood regeneration were definitely verified by the
condition of bone-marrow at necropsy

Purpura and hemorrhage are also associated with acute
leukemias, many of which are of the myeloblastic type   Many
blood slides studied here revealed no evidence of leukemia

The presence of a few myelocytes in the midst of active blood regeneration is not surprising. Neither myeloblasts nor young lymphocytes were at any time noted.

Intestinal hemorrhage is not infrequently found in severe stages of nephritis, particularly in those instances associated with nitrogen retention. This possibility was kept in mind when a blood urea nitrogen of 40 mg per 100 c c was noted soon after admission. However, there was no other evidence pointing to this condition and later a normal reading of 16 mg was obtained. It is likely that the initial increase was due to a dehydration type of retention subsequent to blood loss and lack of fluid intake. In a number of cases of severe nephritis with nitrogen retention we have noted hemorrhage in the absence of disturbance of the bleeding time, coagulation time, platelet count, or clot retraction. In these instances the defect has appeared to be one of the capillary endothelium. The presence of a small carcinomatous ulcer at necropsy demonstrated the site of bleeding. It seems plausible to believe that the presence of thrombocytopenia accentuated the degree of hemorrhage from this area. Another interesting association of malignancy and purpura is occasionally brought about by metastasis to the bone-marrow. Of two instances of carcinoma with thrombocytopenia purpura in a large series of cases of purpura described by Rosenthal,[3] one had such metastasis and the other did not. This was not demonstrated in our patient at necropsy.

Note.—We wish to make acknowledgments to Dr Boerner for personal attention to the hematology in this case.

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SYPHILIS WITH SEVERE ANEMIA*

The presence of severe anemia in a patient with a positive
Wassermann reaction always arouses the speculation as to the
incidence of primary anemia in syphilis, or the possibility of an
anemia peculiar to syphilis (syphilitic anemia) Another source
of confusion is the occasional occurrence of a false positive Was
sermann in pernicious anemia or severe secondary anemia These
questions of interpretation are brought out in the case under dis-
cussion and the practical problem of treatment is forcibly called
to our attention by the possible untoward effects of specific
treatment in such instances

Case History —The patient, Carmello P , is an Italian woman,
forty five years of age She is a widow and has had three chil
dren who are well and three stillborn children at the seventh
month of pregnancy The family history is negative and the
cause of her husband's death was not elicited Previous medical
history is negative Present illness Patient was well until
November, 1925, about nine months before admission At this
time she began to have pains all over the body and became weak
She had particularly severe pain in the lumbar region of the
back, radiating to both sides She then noticed increasing pallor
and the loss of weight of 30 pounds during the period up to ad-
mission into the hospital. About March, 1926, she regained her
normal color, but some time later she again became pale Ap
petite was poor, no nausea, vomiting or soreness of the tongue
Bowels were constipated and she required laxatives constantly,
but stools were normal in color No paresthesias, no pruritus
Menstruation occurred every twenty-eight days and lasted three
to four days but is decreasing in amount

The physical examination is as follows

Central Nervous (Dr Patten) —Pupils very slightly irregular,
but the left is slightly larger than the right, both react to light,

corresponding to five days after the first transfusion and four days after the first dose of neo-arsphenamin However, six days after the second injection of neo-arsphenamin the count fell again, and thirteen days after this dose a definite aplastic state was evidenced by the lowering of the leukocyte count to 2050 and by the progressive sinking of the red cells though some nucleated red cells were still seen On September 25th discrete grayish-yellow spots of exudate were found in the mouth over the fauces Some fusospirillary organisms were found in the smears from these lesions, Bacillus diphtheriae was not present The temperature rose to 103° F about this time and remained continuous and occasionally remittent in type No genital lesions were present such as are noted in agranulocytic angina On September 22d, the eye grounds showed hemorrhagic areas in the macular area The blood-count sank to lower levels with the leukocytes going down to 850, and with no polymorphonuclear cells seen Death occurred on September 30th, forty-four days after admission Necropsy permission was not obtained Among the various therapeutic measures not mentioned above were a high protein and vitamin diet including liver, fresh bone-marrow extracts by intramuscular injection, and stovarsol by mouth

Discussion —In analyzing cases of severe anemia in patients with a positive Wassermann reaction it is helpful to follow Stokes[1] and divide them into three classes 1, True pernicious anemia giving a false positive Wassermann reaction, 2, true pernicious anemia in association with syphilis, 3, severe anemia due directly or indirectly to syphilis Though it is conceivable that by varying methods, false positive Wassermann reactions may be elicited in pernicious anemia, the experience of Kolmer and Steinfield,[2] with various other conditions, has indicated that this should not be a source of confusion, if the Kolmer method is used Stokes has found that severe anemia either primary or secondary has been rare in late or latent syphilis and regards the evidence of relationship of the two diseases as equivocal He rightly emphasizes the necessity of corroboration by clinical evidence of syphilis in these instances It is difficult to estimate the evidence of former investigators

on this subject because of the varying interpretation of what constitutes a diagnosis of syphilis and pernicious anemia For example Hoff[3] includes in a series of syphilitic anemias, 5 patients without a positive Wassermann reaction but in whom the diagnosis of syphilitic aortitis was made by sections from necropsy material He believed that he demonstrated an etiologic relationship between syphilis and pernicious anemia Improvement under iodids was taken to be a criterion of this relationship though the frequent non specific action of this remedy is not unusual In addition, though the response of pernicious anemia to arsphenamin in the absence of syphilis has been the subject of numerous reports, unfavorable results have been noted by Stokes, Winterfeld, and others in the treatment of severe anemias of proved syphilis It is also evident that there is a lack of uniformity in the hematologic and clinical evidence for pernicious anemia particularly in the older literature

Winterfeld[4] believes that an etiologic connection between syphilis and pernicious anemia is not verified by analysis He does, however, believe that syphilis acting on the gastric mucosa in a person predisposed to pernicious anemia may create conditions favoring a "luetic pernicious anemia" Though we are not aware of what characterizes a predisposition to pernicious anemia, one cannot dismiss this hypothesis without considering the occasional instances of families showing tendencies similar in each member in varying degrees such as achlorhydria or achylia and anemia particularly with high color index

Pappenheim[5] also considered that the presence of a disposition toward pernicious anemia in the presence of syphilis might create the picture of pernicious anemia The study of gastric secretion in syphilis and the relation of gastric syphilis to severe anemia merits further study

Piney[6] states that syphilis may produce hematologic changes indistinguishable from pernicious anemia Occasionally severe anemias in the tertiary stages of syphilis are associated with hepatic syphilis Probably one of the most convincing reports is that of Naegeli[7] A patient of his, seen in 1898, with definite pernicious anemia and tertiary syphilis, under arsenic and mer-

cury recovered and remained well until the last observation in 1918 This would make an unusual remission for pernicious anemia—nearly twenty years

The reports of results of treatment in syphilis with severe anemia have not been always favorable The aplastic picture noted in the case under discussion is analogous to a number of reports in the literature This complication as well as hemorrhagic manifestations are particularly likely to occur with sulpharsphenamin and neo-arsphenamin Similar instances are described by Gorke [8] One of his patients after a course totalling 2 85 gm of arsphenamin developed necrotic areas on the tonsils, purpuric spots on the legs and the blood-count sank down to red blood-cells 900,000, hemoglobin 13 per cent, white blood-cells 600, and platelets 10,000, bleeding time was thirty minutes Winterfeld cites the history of a man aged forty-two years with a history of syphilis of two years' duration, the blood-count was red blood-cells 1,325,000, hemoglobin 33 per cent, white blood-cells 2500 After several small doses of arsphenamin, a febrile reaction occurred and the blood-count fell rapidly until the patient succumbed Foucar and Stokes[9] also have noted unfavorable results with arsphenamin treatment in primary and secondary anemia in the presence of syphilis Moore and Keidel[10] described an aplastic reaction with necrotic ulcers on the hard palate, purpuric spots, hemorrhagic symptoms and death in a woman fifty years of age after the eleventh dose of neo-arsphenamin These reactions may be interpreted in several ways, either as an idiosyncrasy to arsphenamin per se, or a form of visceral Herxheimer reaction with the liberation of myelotoxic substances

Differential Diagnosis —Though some of the reported cases of anemia in patients with syphilis approximate the clinical and hematologic picture of pernicious anemia, the case under discussion offers no difficulty in this respect With few exceptions, the blood-counts showed a color-index below 1, the diameter of the red cells was within normal limits and the volume index was below 1 No megaloblasts were found though normoblasts were seen in small numbers There was free HCl in the gastric con

tents and the neurologic findings were not characteristic, particularly the presence of vibratory sensation The high indirect van den Bergh readings are of course also found in pernicious anemia and suggest that blood destruction was increased in this instance

In favor of the possibility of gastric syphilis, there are present certain features particularly in the roentgenograms which fulfil several of the requirements for this diagnosis outlined by Eusterman and Carman [11] A filling defect was present without a corresponding palpable mass, a tube like deformity with little or no peristaltic waves suggested the stiffening or rigidity of the pylorus and prepyloric region The loss of weight though supposedly characteristic of malignancy may be quite marked in gastric syphilis The presence of achlorhydria or achylia is not unusual in gastric syphilis and it is possible that the pathogenesis of severe anemia in syphilis is comparable to that of pernicious anemia

The likelihood of gastric malignancy in co-existence with syphilis cannot be arbitrarily dismissed in the absence of a necropsy The lack of a characteristic x ray picture and the negative reactions for occult blood in the stools weigh somewhat against this diagnosis

The aplastic reaction and the throat lesions noted after treatment are no doubt comparable to those described in the literature Agranulocytic angina occurs in middle aged women who were previously presumably normal and though the leukopenia is profound, the red cells and hemoglobin may not be greatly reduced In addition to the necrotic lesions in the mouth, there are similar exudates on the genitalia These genital lesions were absent in this patient

Though we cannot, strictly speaking, draw conclusions from a single case, there are several features of interest which merit further study The question of the relation of gastric syphilis to severe syphilitic anemias and the search for a more uniformly successful method of handling these patients are particularly pertinent. It appears to be preferable to use liver and a high vitamin diet, blood transfusions and other measures of symp-

tomatic nature such as dilute hydrochloric acid in an attempt to improve the anemia before the cautious use of neo-arsphenamin

TABLE I

1926	R. B C	Hb per cent	W B C.	Polys	S L	L L	Monocytes	Eosin	Remarks
8/17	1,720,000	28	9,100	43	32	18	7		
8/20									Pot bism tartrate 0 1 gm
8/23	2,100,000	35	7,300	48	33	9	8	2	
8/27	1,820,000	25	6,400	54	25	10	7	4	Pot bism tartrate 0 1 gm.
9/3	2,110,000	35	9,200						Transfusion 9/2, neo-arsph 0 3 gm
9/7	3,210,000	37	7,300	45	26	25	2	2	Neo-arsph 0 3 gm
9/13	1,170,000	20	7,050	56	27	15	2		
9/14	1,150,000	22							
9/20	1,280,000	29	2,050	16	66	17	1		Transfusion 9/19 Fever to 102° F
9/24	1,090,000	23	1,000	24	76				Neo-arsph 0 3 gm 9/22
9/27	900,000	19	850	0	90	10			

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CLINIC OF DRS HARRY SHAY, HENRY TUMEN, AND ISADORE RODIS

FROM THE GASTRO-INTESTINAL CLINIC OF THE JEWISH HOSPITAL

THE DIAGNOSIS OF GALL-STONES RELATIVE ACCURACY OF CHOLECYSTOGRAPHY AND NON-SURGICAL BILIARY DRAINAGE

JANE WELSH CARLYLE, when stricken with influenza during the great epidemic in 1847, made the accusation that medical men have entered into a tacit agreement to call all sorts of cold weather ailments by the same name so that their practice might be greatly simplified This almost holds true for the frequency with which the diagnosis of gall bladder disease is made and the flimsy evidence upon which these diagnoses are often based

Judd[1] found that in 83 per cent of a group of patients in whom gall bladder operation was attended with poor results, the clinical history of attacks of colic was not clear That even a so-called "typical gall bladder attack" may not be due to gall-bladder disease is shown by the following case

M G , female, age thirty nine years, reported to the gastro-intestinal clinic with a history of belching, postmeal gaseous distress, occasional heartburn, and constipation lasting over a period of four or five years At irregular intervals, she complained of pain in the epigastrium with radiation to the back and right shoulder At no time had the attacks of pain been severe Before her study at the clinic could be completed, she was admitted to the hospital during an exacerbation similar to the above, but much more severe in character than any she had experienced previously When the acute symptoms had subsided, operation was performed, but the gall bladder was found to be perfectly normal in appearance and to touch

TABLE I

Case No	Age	Sex.	No of exam	Bile centrifuged.	Chol crystals	Pigment	Cystic duct *	Diagnosis by drainage	Operative diagnosis.
1	23	F	1	+	+	+	P	stones	stones
2	48	F	1	−	−	+	P	stones	stones
3	45	F	2	+	+	−	P	stones	stones
4	49	F	1	−	−	+	P	stones	stones
5	46	F	1	−	+	+	P	stones	stones
6	24	F	1	−	−	+	P	stones	stones
7	43	F	1	−	+	+	P	stones	stones
8	60	M	3	−	+	+	P	stones	stones
9	29	F	1	−	+	+	P	stones	stones
10	36	M	1	−	+	+	P	stones	stones
11	42	F	1	+	+	+	P	stones	stones
12	55	F	1	−	−	+	P	stones	stones
13	26	F	1	+	+	+	P	stones	stones
14	48	F	1	−	−	+	G B removed	stones	stone in duct (hepat.)
15	24	F	1	−	+	+	P	stones	stones
16	26	M	1	−	+	+	P	stones	stones
17	45	M	1	−	+	+	P	stones	stones
18	32	F	1	+	+	+	P	stones	stones
19	21	F	1	−	−	+	P	stones	stones
20	68	F	1	+	+	−	P	stones	stones
21	52	F	1	−	+	−	P	stones	stones
22	47	F	1	+	+	−	P	stones	stones
23	52	F	4	−	+	+	P	stones	stones
24	42	F	15	−	−	−	P	no stones	no stones
25	30	F	1	−	−	−	P	no stones	no stones
26	36	F	2	−	−	−	P	no stones	no stones
27	33	F	1	−	−	−	P	no stones	no stones
28	55	F	2	−	−	−	P	no stones	no stones
29	50	F	1	−	−	−	P	no stones	no stones
30	26	F	1	−	−	−	P	no stones	no stones
31	63	F	1	−	−	−	P	no stones	no stones
32	54	F	1	−	−	−	P	no stones	no stones
33	24	F	1	−	−	−	P	no stones	no stones
34	28	F	1	−	−	−	P	no stones	no stones
35	35	F	8	−	−	−	obs	no stones	stones
36	40	F	4	−	−	−	obs	no stones	stones
37	42	F	2	−	−	−	obs.	no stones	stones
38	22	F	3	−	−	−	obs	no stones	stones

* Cystic duct P = patent obs. = obstructed.

It is true in many cases of gall bladder disease the experienced physician can readily, by means of the history and physical examination reach a correct conclusion. We believe, however, that there is a larger group of cases which present digestive disturbances and tenderness in the epigastrium or right hypochondrium in which an accurate localization of the existing pathology is well nigh impossible without the aid of other diagnostic measures. One can hardly speak of the symptomatology of gall bladder disease, except perhaps in those who experience typical colic, without keeping in mind the array of similar symptoms which may manifest themselves in patients with neurasthenia, constipation, spastic colitis, visceroptosis, disturbances in gastric secretion, pancreatic insufficiency, and many others.

The past ten years has seen the introduction of two procedures which have been advocated as aids in the diagnosis of gall bladder disease. These are non-surgical biliary drainage and cholecystography. Since its introduction four years ago, the latter has greatly outdistanced its predecessor in popularity. The frequency with which cholecystography is used today is evidence that a good history and physical examination do not always suffice to make an accurate diagnosis. We propose to point out in this paper the relative values of non surgical biliary drainage and cholecystography in the diagnosis of cholelithiasis. This study is based only on cases that were operated upon.

During the past year we have performed non-surgical biliary drainage upon 38 patients who were subsequently operated upon. Table I includes the drainage and operative findings.

Table I.—An analysis of this table will reveal several interesting findings. Of these 38 cases, a diagnosis of stones was made from the bile examination in 23 and of absence of stones in 11. In 4, a diagnosis of cystic duct obstruction was made because of the absence of "B" or gall bladder bile on repeated drainages. No opinion regarding the presence or absence of stones could be given because of this fact. At operation in these 4 cases the cystic duct was found occluded by a stone. The diagnosis in the remaining 34 cases was confirmed at operation. It is in the comparatively small group of cases, where the cystic duct is oc

cluded, that non-surgical drainage fails to give accurate data regarding the gall-bladder contents   A further source of error in this group may also arise if the portion of the cystic duct adjacent to the gall-bladder is not involved in the obstruction This is the only portion of the duct system which has the power of concentration[2] and may thus produce a concentrated bile A correct diagnosis of the presence or absence of stones was made in 89 5 per cent of the series studied by bile drainage alone   It is of interest to note that in the vast majority of cases only one drainage was done   In 6 cases the diagnostic elements were found only after centrifuging the bile obtained   In many instances the bile was presented for study before the patient was seen by the examiner

Of these 38 cases, 24 were cholecystographed prior to operation

This group included 18 stone and 6 non-stone cases   A comparison of diagnoses made by non-surgical biliary drainage and by x-ray is shown in Table II

In analyzing these 24 cases it is to be noted that non-surgical biliary drainage failed to indicate stones in 3 of 18 stone cases, an error of 16 6 per cent   In this same series stones were visualized by oral cholecystography in only one and reported as suspiciously present in a second one, an error of 88 8 per cent Since this study is limited only to the diagnosis of stones, it must be stated, in all fairness to the x-ray that in many of this series, an abnormally functioning gall-bladder was diagnosed, even though in most instances the contained stones were not visualized

Of the non-stone cases, all were so diagnosed by non-surgical biliary drainage   Cholecystography made a false diagnosis of stones in one of these or an error of 16 6 per cent in the negative series

From these findings several important facts should be emphasized

First, in no case where gall-bladder bile was obtainable by drainage was an incorrect diagnosis of the presence or absence of stones made   The 3 cases in which bile drainage failed to diag

TABLE II

	Diagnosis made by		
	Bile drainage	Cholecystography (oral)	Operation.
1	stones	negative	stones
2	stones	negative	stones
3	stones	negative	stones
4	stones	stones?	stones
5	stones	negative	stones
6	stones	negative	stones
7	stones	negative	stones
8	stones	negative	stones
9	stones	negative	stones
10	stones	negative	stones
11	stones	negative	stones
12	stones	negative	stones
13	stones	negative	stones
14	stones	negative	stones
15	stones	negative	stones
16	no stones	negative	stones
17	no stones	negative	stones
18	no stones	stones	stones
19	negative	stones	negative
20	negative	negative	negative
21	negative	negative	negative
22	negative	negative	negative
23	negative	negative	negative
24	negative	negative	negative

nose stones when present belong to the cystic duct obstruction group in Table I

Second, in this series at least, oral cholecystography was a very disappointing diagnostic measure of the presence of gall-stones   Were we considering the diagnosis of abnormal function as well, our false negative x-ray findings would probably compare with Eusterman's[3] 30 per cent error   However, considering stones alone, the error is much greater

Third, in no case was a false positive diagnosis made by drainage, while such an error did occur by cholecystography

False positive cholecystographic findings were recently reported by Kirklin [4]

Such false data have been reported even with the intravenous technic in the presence of severe liver disease[5] and in patients with easy fatigability, achlorhydria, and low basal metabolic rate

Diagnosis by Non-surgical Drainage —The technic of non-surgical biliary drainage need not be described here, as it may readily be obtained from Lyon's book [6]   Further we do not intend to enter into any controversy as to whether the "B" bile is gall-bladder bile or whether the gall-bladder is capable of emptying itself or whether magnesium sulphate, which we used routinely as a stimulant in our diagnostic studies, is capable of causing gall-bladder evacuation   These questions have all been discussed in the literature [2, 7, 8]   We believe that when a fraction of bile is obtained after magnesium sulphate stimulation, varying in color from a medium brown to a black brown or black green and in amount from 30 to 50 c c , we are dealing with a gall-bladder that has retained its function of concentration Further that the recovery of such a fraction indicates that the capacity of the gall-bladder to empty is not seriously impaired Finally the cystic duct must needs be patent at least in part to permit the gall-bladder to evacuate its contents

The presence of stones is determined by the microscopic examination of the bile   The findings upon which the diagnosis is based have been indicated previously by one of us [9]   Jones"[10] article contains an excellent plate illustrating these, but that author failed to stress their diagnostic importance   Further experience with these findings has led us to believe that the mi-

croscopic demonstration of the typical calcium bilirubinate pigment and cholesterol crystals in drainage bile is pathognomonic of stones or their precursor, sand

The crystallization of cholesterol, in square or slightly oblong clear crystals, many with one corner chipped off in the form of a perfect right angle, is so characteristic as to defy improper identification The pigment, however, upon which we lay so much stress, requires a little practice to recognize It must be differentiated from other pigment bodies which may be found in the bile Dense clumps of precipitated bile salts, bile stained bacteria or mucus and degenerated cells, may be confusing to the inexperienced This pigment appears as brilliant golden yellow to orange colored granular clumps

In the present series, we have found the presence of either the pigment or the crystals alone sufficient to warrant a diagnosis of stones In 6 cases pigment alone was found and in 4 crystals alone All these proved to be stone cases at operation In one instance, a stone in the duct was diagnosed after a previous cholecystectomy had been done This was confirmed by operation (Case 14) When crystals alone are found the possibility of cholesterosis of the gall bladder must be considered, but thus far we have not encountered such an instance

In conclusion, we wish again to stress the importance of the above findings in drainage bile, as a diagnostic aid in gall-stone disease. We desire to emphasize the fact that the above findings like other specific laboratory data are of considerable importance when positive It is evident that even by the most careful examination of the bile, the presence of only minute amounts of crystals or pigment may be overlooked However, in our experience, when found, these elements have proved to indicate stones Finally, the finding of these elements in the bile has proved to be far superior to oral cholecystography as an aid in the diagnosis of gall stones

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ANGINA PECTORIS

ANGINA pectoris was first brought to the general attention by William Heberden [1] A short excerpt from his classical description merits quotation "Those who are afflicted with it, are seized, while they are walking, and more particularly when they walk soon after eating, with a painful and most disagreeable sensation in the breast, which seems as if it would take their life away, if it were to increase or continue, the moment they stand still all this uneasiness vanishes" He called attention to the substernal location and brachial radiation of the pain, the absence of dyspnea, and the tendency to sudden death, and christened this group of symptoms "angina pectoris"

The syndrome seems to be becoming definitely more prevalent. We do not know what factor is responsible for this Donnison's statement [2] that he has never seen a case of angina pectoris among the natives of Kenya colony (Central Africa) is very striking Houston [3] likewise reports the absence of this condition among the Chinese The consensus of opinion of these and other authors [4] seems to be that on account of the rate at which we live, rather than because of any dietary, climatic, or other factor, our cardiovascular systems degenerate more rapidly than those of less energetic peoples The increasing prevalence of angina is therefore possibly attributable to our ever-increasing rate of living, and the increased tendency to cardiovascular degeneration which it seems to carry in its wake

CLINICAL PICTURE

Angina pectoris is seen most frequently in men past forty years of age   It is apt to choose its victims from among those carrying heavy responsibilities, particularly from the ranks of our own profession, although the laboring class is by no means exempt   Frequently the onset is preceded by a period of high nervous tension and worry   This was recently impressed upon us in the case of the proprietor of a gambling house who developed angina when the even tenor of his life was disturbed as a result of a spasm of virtue on the part of the prosecuting officers of his city

There are, as a rule, no *prodromes* to an attack   The case reported by Osler[5] in which profuse sweating preceded the onset by half an hour is exceptional

The *exciting cause* is characteristically exertion, usually physical, sometimes mental, usually after eating, more particularly when the exertion occurs out of doors   The combination of physiologic events incident to getting up to make an after-dinner speech has frequently excited anginal attacks   Walking up hill against a cold wind is another undertaking particularly likely to provoke an attack   Anginal pain often comes on during sleep, but usually in those cases in which it also accompanies exertion   It is well to be cautious in the diagnosis of angina pectoris when the attacks bear no relation to bodily activity, but this type does occur in the case of tobacco angina   Allbutt[6] stated, however, that in his experience the symptoms of tobacco angina differed from those of the usual variety, so it may be due to a different mechanism

The *pain* may be mild, a mere sense of pressure or constriction   Patients often describe it as a mild indigestion, on account of its frequent association with flatulence, and its relief by belching   It may be absent in cases of so-called "angina sine dolore" (attacks of sudden arrest and angor animi, without pain, seen in some anginal patients alternating with true attacks)   On the other hand, the pain may be terrific and overpowering, as though the chest were being crushed in a huge vise

Stabbing, burning, and needle-like pain should arouse our skepticism

The *location* of the pain is not characteristically "precordial," as it has sometimes been termed. It is true that it may be located anywhere in the chest, arms, neck, or upper abdomen. In fact, Osler[3] has described extrapectoral forms in the scrotum and legs. We have had one case in which pain was first noted just above the left eye. However, in the vast majority of cases of undoubted angina pectoris the primary and main focus of pain is beneath the sternum, usually beneath the upper, but often beneath the lower part of this bone. From this point it may radiate to the arms, neck, and back. Occasionally it starts peripherally and ends centrally. Many patients are able to describe in minutest detail the spread of their pain.

The *"angor animi"* may or may not be present in an attack. Frequently one feels tempted to attribute this symptom to the conscious or subconscious fear on the part of the patient that his heart will stop. That this is not always the case is indicated by the fact that this sense of ill-omen is sometimes present when the anginal pain is confined to the arm, in persons who do not recognize the relation of this brachial pain to their cardiac function. It is well to remember that during the attack the patient is usually not frightened in the ordinary sense of the word, but is rather awe-struck.

Immobilization occurs in the vast majority of anginal attacks, whether the pain is mild or severe. Some patients, however, give the history that if an attack comes on when they are walking, slowing their pace will bring relief. Following this initial "pull up," they can undertake considerable exertion without bringing on an attack. Wenckebach[7] has called attention to the analogy which exists between this type of angina and the substernal oppression occurring in athletes at the beginning of a contest, which is relieved by the "second wind." Occasionally, restlessness supervenes toward the end of a long attack of pain, but its occurrence must raise the question of a coronary occlusion. Cases of tobacco angina are said to become panicky and restless during the pain, in this respect simulating the be-

havior of neurotic women in a vasomotor storm   This was true in our most clear-cut case of tobacco angina

The *position* assumed in an attack is usually the sitting one Sometimes the patient stands   Recumbency frequently seems to exaggerate and prolong the pain

Dyspnea is usually absent during the attack   The chest is held almost immobilized   Shallow breaths are taken lest deep breathing increase the distress   Seneca is named by Osler[5] as having possibly penned the earliest description of angina pectoris In a letter to Pliny[8] he refers to attacks from which he was then suffering, which came on "like a storm" and were accompanied by a sense of impending death   "To have any other malady is only to be sick, to have this one is to be dying" However, he refers to excessive "sighing" and dyspnea accompanying his attacks, a fact which makes one skeptical as to their being angina pectoris   Occasionally, however, we have seen paroxysmal cardiac dyspnea associated with anginal pain A rather unusual respiratory feature was presented by a patient under our care, who could postpone the onset of an attack while walking by deep breathing

Cardiovascular Phenomena —Many observations are on record of the behavior of the *pulse* during the attack   Mackenzie[9] was able to obtain a considerable number of polygraphic tracings to illustrate its action   Sometimes the rate is markedly accelerated, sometimes it is slowed, often it is unchanged, but usually there is an acceleration of 10 or 15 beats per minute during the pain   Irregularity is unusual, and when it occurs is a bad prognostic sign   Osler[5] has reported the appearance of a difference in the radial pulse of the two arms during the seizure Occasionally the pulse has been noted to disappear entirely during a severe paroxysm, and return subsequently, though the heart sounds continued to be audible throughout

The *heart sounds* are usually unchanged during the attack, except as regards the rate   Huchard[10] has reported a case in which a systolic murmur developed during the attack, and disappeared afterward, but this is an unusual observation

No definite rule can be formulated concerning the behavior

of the *blood pressure* during the attack Usually there is an elevation of 20 mm or more in the systolic pressure Sometimes a much more marked rise occurs Sometimes the pressure does not vary and occasionally it falls In the majority of our cases the moderate rise during the attack gave place to a fall when the pain subsided

Electrocardiographic tracings taken during attacks of angina pectoris are not very plentiful Bousfield,[11] and Ful and Siegel[12] have published such tracings Bousfield's case showed a most remarkable change in the ventricular complex which disappeared when the pain subsided We have obtained several tracings during the past year (to be published) Some of these show no change, but the majority show quite definite alterations in the shape of the Q R S and T waves, or of the S T interval, which cannot be attributed to the rate changes observed The resemblance of these tracings to some we have taken of dogs and cats with temporary experimental coronary occlusion is quite striking

Reports of *fluoroscopic observations* of the heart during anginal attacks are even rarer than electrocardiographic tracings Two have come to our knowledge In one[13] no change was observed in the size or action of the heart In the other[14] a "krampfhafte Zuzammenziehung' of the cardiac shadow was reported We have had one opportunity to make such an examination, and were able to see no change in the cardiac silhouette during the pain

Certain agents *are known to bring relief from the attack itself* Of these agents, *rest* and *immobility* in the sitting or the standing position come first The *nitrites*, which have been used widely for this purpose since they were introduced by Lauder Brunton,[16] are frequently disappointing In many cases however, they bring about a very definite cessation of pain, coincident with a sudden drop of blood pressure of 40 to 60 mm, which occurs within thirty or forty seconds Sometimes, when the blood pressure rises again after three or four minutes, the pain returns Often in spite of a fall of pressure, the pain continues unabated *Belching* is often regarded by the patient as an effi-

cient agent in the relief of angina pectoris   Some are able to obtain quite as satisfactory relief from aromatic spirits of ammonia as from nitroglycerin or amyl nitrite   Wenckebach[7] cites one other agent which he says produces a cessation of the pain, i e , the sudden onset of a paroxysm of tachycardia or fibrillation during the attack   The occurrence of chronic auricular fibrillation or congestive failure usually has the compensating virtue of freeing the patient from anginal attacks   From this point of view the following case has interested us   A physician who was subject to asthmatic bronchitis and repeated attacks of severe angina, gradually developed a tendency to slight congestive failure   His angina disappeared at this point, but he then began to have paroxysms of auricular fibrillation   Recently, following improvement in his bronchial condition, the tendency to congestive failure has disappeared, the anginal attacks have returned, and there have been no further paroxysms of fibrillation   Mackenzie's opinion[9] that the development of congestive failure prevents the patient from carrying his exertion to that point necessary to produce angina pectoris is worthy of note, but does not seem to explain the circumstances in this case or in some others we have studied   The congestive failure was so slight that our patient was able to undertake almost as much exertion as before, and quite as much as that which is now productive of an attack

The *mode of death* in an anginal attack is worthy of careful consideration, since its mechanism has been the subject of some dispute   Few men have the opportunity to observe personally many deaths of this type   In the past the so-called "status anginosus," now believed to be due, as a rule, to coronary occlusion, was confused with true angina, and death in this condition was frequently cited as an example of anginal death   When we eliminate this error we find, on the basis of reports of competent observers, that death during the attack occurs as a rule in one of two ways   First, the pulse may stop abruptly, without any previous irregularity or any change in rate of strength—a gasp or two and the patient is dead   This type of cardiac arrest is often seen early in the attack   Second, the pulse may

become weak and irregular, especially toward the end of a long attack, and then suddenly stop There is no certain knowledge as to whether the whole heart stops suddenly, or whether it goes into ventricular fibrillation It may be that the first type of cardiac arrest mentioned is a sudden stopping of all chambers, whereas the second is a ventricular fibrillation If we were able to obtain electrocardiograms during or shortly after death in angina pectoris, we might be able to solve this much disputed and important problem

There is one careful and most interesting account by Osler[5] concerning the mechanism of cardiac arrest The patient suddenly collapsed, no pulse was felt in brachials or carotids, and no heart sounds were audible Osler thrust a long needle into the heart and observed a definite cardiac impulse at a rate of 52 per minute The impulse gradually slowed, and stopped fifty minutes after the onset of the collapse The author stated that the beat showed no irregularity nor tremor such as one would expect if the heart were fibrillating The case is most puzzling

ETIOLOGY

In Heberden's classical account[1] of this "disorder of the breast" we find the following statement "What the particular mischief is, which is referred to these different parts of the sternum, it is not easy to guess, and I have had no opportunity of knowing with certainty" A hundred and sixty years later we have to admit to much the same ignorance Students of this subject may be grouped into two main schools The first of these holds that angina pectoris is a symptom, which may be caused by one of several pathologic lesions, because the variable clinical findings during the attack and the variable postmortem observations do not bear out the hypothesis that a single lesion is reponsible in all cases The second school holds that angina pectoris is caused by a certain definite pathologic lesion and is, therefore, a disease entity and not a mere symptom This school may be subdivided according to the lesion supposed to be responsible for the attacks

First of all there are those who uphold what is known as

the *coronary hypothesis,* that the pain is due to coronary artery disease   Their chief arguments are that this lesion is found in the vast majority of patients dying of angina pectoris, and that coronary occlusion produces a clinical picture somewhat comparable to that of angina, in fact, often indistinguishable from it   Sir Edward Jenner probably originated this hypothesis In a letter to Parry,[16] he describes the striking of his knife against something "so hard and gritty as to notch it," one day when opening the heart of a patient who had died of angina pectoris He says "I well remember looking up at the ceiling, which was old and crumbling, conceiving that some plaster had fallen down   But on further scrutiny the real cause appeared   the coronaries had become bony canals "   How coronary artery disease produces pain has been variously explained   Parry[16] was probably the first to remark that "though a quantity of blood may circulate through these arteries, sufficient to nourish the heart, as appears in some instances, from the size and firmness of that organ, yet there may probably be less than what is requisite for ready and vigorous action   Hence, though a heart so diseased may be fit for the purposes of common circulation during a state of bodily and mental tranquillity, and of health otherwise good, yet when any unusual exertion is required, its powers may fail, under the new and extraordinary demand " This may be termed the "intermittent myocardial ischemia hypothesis "   Keefer and Resnik[17] in a recent paper, have extended this hypothesis somewhat, to include other causes of insufficient myocardial blood-supply, such as aortic regurgitation,* and anemia   Herrmann[18] has given us a coronary explanation for angina in mitral stenosis   He describes the occurrence in this condition of an atrophy of the pad of fat, which is normally found beneath the circumflex branch of the left coronary artery, and a thinning of the vessel wall at this point, "so that any sudden increase of intra-auricular pressure could obliterate the artery or narrow it considerably, and seriously embarrass the circulation of the heart "

* This lesion is presumed to act by lowering diastolic intra aortic pressure thereby interfering with proper coronary filling

However, this myocardial ischemia hypothesis has to contend with the fact that the myocardium is probably insensitive. The origin of the pain has, therefore, been variously attributed to (1) Coronary spasm, (2) inco ordinate action of the various parts of the heart with consequent stretching of its investments, (3) anoxemia of the pericoronary sensory fibers, (4) dilatation of the heart, and (5) abnormal contraction of the heart muscle. All of these variations of the coronary hypothesis have this in common: that they postulate an anoxemia of a section of the myocardium as the cause or as an accompaniment of the pain, and attribute death to ventricular fibrillation resulting from this myocardial ischemia.

The *aortic hypothesis* owes its origin to Sir Clifford Allbutt.[19] He was dissatisfied with the coronary hypothesis because it did not explain the occurrence of angina pectoris in patients with no postmortem evidence of coronary disease. Moreover, he pointed out that "amid the agitation of patient and attendants, the heart, assumed to be the protagonist in the conflict, often seems to be the one impassive actor." He compared this im passive heart action, and the behavior of the blood pressure dur during anginal attacks with the irregularity of the action of a dog's heart in the presence of sudden myocardial ischemia, and the fall of blood pressure which is almost invariably observed in such experiments. His hypothesis states that anginal pain is due to distention of a diseased "suprasigmoid" aorta and that death results from vagal inhibition, "the vagus stung by the pain, acting often upon a decrescent heart." The coronary disease so frequently found postmortem has nothing to do with the pain, but "determines the mortal issue," since a normal heart will not usually stop permanently as a result of vagal inhibition. Recently Wenckebach[7] has expanded this hypothesis. Aortic distention is held to be the usual mechanism of the production of anginal pain, but sometimes the pain may be due to the stretching of a diseased coronary artery, and occasionally even of a mesenteric vessel. Wenckebach attributes death in angina to ventricular fibrillation as a result of the heart attempting to pump blood against a continued high and rising blood pressure.

It is analogous to the fibrillation produced in an experimental animal by clamping the aorta

Spasm of the aorta, and neuralgia of the cardiac plexus are two other suggestions which have been proposed to explain the etiology of angina pectoris   They are difficult to prove, but not as yet disproved

In attempting to decide for or against these various hypotheses the results obtained by animal experimentation merit discussion   Without going into detail we can state with a fair amount of assurance that stimulation of the endocardium and myocardium probably does not produce pain, that the pericardium and epicardium may be moderately sensitive, especially in the aortic region, and that severe pain, similar in nature to that seen in a full-blown attack of angina pectoris, is produced in animals by stimulation of sensory fibers which lie in the adventitia of both the aorta and the coronary vessels [20, 21, 22]

Clinical evidence supplements these observations   Coronary thrombosis on the one hand, and aortic rupture on the other, both may give rise to intense pain, comparable in type to that of angina pectoris   The pain of these conditions is usually more severe and more shocking than anginal pain, and in coronary occlusion its location is apt to be lower in the chest   Nevertheless, these two clinical pictures show that sensory nerves probably occur in these two regions in man as they do in dogs and that severe pain is produced by stimulation of them

Postmortem studies of angina pectoris are not apt to give us a definite answer to the question of etiology because the disease consists of a series of attacks which cannot be studied pathologically   Nevertheless, after death we can observe those morphologic changes, in the presence of which attacks may arise   These are, in the vast majority of cases, *coronary sclerosis*, and *aortic disease* (aneurysm, aortitis and aortic regurgitation) often syphilitic   In patients dying of angina pectoris these changes may be present separately or together   They may, however, both be present in patients who never had an attack Very occasionally neither of them is found postmortem in an individual who has had the most typical anginal seizures [23]

The evidence for this last statement has been presented by competent authorities,[5, 23] and cannot be thrown out of court as it has been in the past by authors attempting to build up a case to support a certain hypothesis

Taking into consideration the above facts, and realizing that the clinical picture of angina pectoris is variable, particularly with regard to the behavior of the circulation, and the location of the pain we incline to the view that some angina is coronary but that some is very probably aortic in origin There may be still other mechanisms occasionally responsible for attacks in some patients, but most angina pectoris seems explainable by one of these two hypotheses This seems to be the trend of current opinion concerning the etiology of this syndrome[24]

If this present tendency of belief is correct, the most important points for us to determine are, first, what proportion of cases are coronary and what proportion are aortic, and second how can we differentiate clinically between the two The importance of these discoveries would lie in the fact that treatment of each type would be different. Thus in aortic angina if we could put an end to the pain (by surgical measures), the danger from the disease would be almost negligible, whereas if we removed the pain in a coronary case we might be doing away with a warning signal, of utmost importance in preventing exertion sufficient to produce ventricular fibrillation and death[9]

The question therefore arises as to how we might attempt to differentiate coronary from aortic angina?

1 Possibly by the location of the pain Rupture of the first portion of the aorta seldom, if ever, produces lower sternal or submammary pain As our knowledge develops, pain low in the chest or in the epigastrium may be found to be coronary in origin.

2 Possibly by the effect of nitrites It is far from clear at the present time why some cases are relieved by nitrites and others fail to be benefited We may find that aortic angina is relieved by this means, whereas the coronary type is not.

3 A more careful study of blood pressure and the correlation

of its behavior during the attack with other data, may be of value

4 Possibly the electrocardiograph may be relied upon to show evidence of ischemia of a section of the myocardium in most coronary cases   Aortic stretching would not seem to be productive of a change in the ventricular complex

5 Cardiac irregularities may be found to be an evidence of coronary angina   However, our experimental observations do not agree with those of other workers, in that we have seldom seen cardiac irregularity in experimental coronary occlusion of short duration   It occurred in our experiments only after the ischemia had lasted for a considerable period of time, just before the ventricles began to fibrillate   It would, therefore, not necessarily be seen during a short temporary myocardial ischemia, such as that postulated by coronarians

6 Fluoroscopic examination, if sufficient data can be accumulated, may help to solve this question, since judging from observations on dogs, it seems that ischemia of a suitably situated section of the myocardium should cause changes in the cardiac action which should be noticeable under the fluoroscope

If some or all of these observations could be made on a sufficient number of cases of angina pectoris, and then correlated with the pathologic findings, we should some day be able to prove or disprove our speculations

DIFFERENTIAL DIAGNOSIS

We do not intend to discuss this subject in detail, but rather to make reference to some of the conditions which have recently presented themselves in our personal experience as demanding differentiation from angina pectoris   The differential diagnosis of this syndrome is somewhat clouded by the fact that we probably include two or more pathologic mechanisms under this name   Formerly coronary occlusion was also a part of this chaos of cardiac pain, and added markedly to the confusion   Since Herrick's paper in 1912[30] we have been learning more and more about the recognition of this accident   Most cases of the so-called "status anginosus" are due to coronary occlusion

Nevertheless when the condition is not accompanied or followed by fever, leukocytosis, pericardial friction typical electro-cardiographic signs of coronary occlusion or prolonged depression of the circulatory function the differential diagnosis may be impossible. In this connection we cite the following case.

A woman sixty seven years old had suffered with extreme hypertension for more than twenty years. During the last two years there had been many anginal attacks some brought on by exertion, others occurring spontaneously. These pains were relieved by nitroglycerin. One evening, while walking back to her apartment after a fairly hearty supper, she was seized with agonizing substernal, precordial, and left brachial pain which was not relieved by nitroglycerin. When one of us saw her an hour later the pain was still shocking in character, the systolic blood pressure had dropped from the customary level of over 250 mm of mercury to 170. Later it dropped to 130. The lungs rapidly filled with moisture. It required $\frac{3}{4}$ of a grain of morphin to relieve the pain. The next morning the lungs were still markedly congested and when the effects of the morphin wore off, pain recurred. The circulation was in a precarious condition. It seemed certain that coronary occlusion had occurred. Nevertheless, following venesection and the withdrawal of 500 c.c. of blood, the pain was immediately relieved, the lungs began to clear, and by the next day the blood pressure had returned almost to its customary level. The rapid recovery rendered the diagnosis uncertain. Following this severe seizure, angina pectoris occurred more frequently than before, and six months later the patient died suddenly in an attack. Levy[23] has recently reported an instructive case in which the diagnosis of coronary obstruction was made clinically on what seemed to be adequate grounds. Following the supposed thrombosis there were numerous anginal seizures. The patient died during an attempt to relieve him by operation on the cervical sympathetic. Necropsy showed no coronary nor aortic disease.

The more continuous types of precordial or substernal pain should be differentiated from angina pectoris, although the dividing line is sometimes very indistinct. A patient with a

blood-pressure of 200/130 is at present under our care   Her hypertension dates back to her menopause twelve years ago During the past five years her husband has been having attacks of paroxysmal auricular fibrillation, which, at his age of seventy-five, must be considered important to abort   She has consequently been under a very severe nervous tension and has had considerable physical exertion while nursing him through these attacks   Since the appearance of his paroxysmal fibrillation she has frequently noticed a sense of discomfort and moderate pain in the second and third left interspaces, 4 or 5 cm from the sternum   This sensation is apt to appear during one of her husband's attacks, and tends to be relieved when the nervous tension relaxes, when physical exertion is reduced and when the bowels are purged with castor oil   This type of discomfort can be differentiated from true angina by the fact that it is more continuous   It may be located almost anywhere in the precordium, and is occasionally confined to the left arm alone Osler[5] termed it the "hot box," since hypertensives tended to develop it when they lived at too rapid a pace   We agree with his statement that this discomfort may, but does not, as a rule, develop into true angina

An apical sense of weakness or heaviness of a slightly different nature is frequently seen   It seems to be due in some way to myocardial fatigue and is not uncommon in mitral stenosis   It has been attributed to stretching of the cardiac investments Hyperesthesia of the precordium and often of the back[24] may accompany it   This type of pain is also of a more continuous nature than true angina

Tobacco may produce precordial distress, usually mild and often apical in location   Occasionally, however, it may give rise to severe angina pectoris, although often these attacks differ in some respects from true angina [6]

Rupture of an aortic valve has recently been reported and discussed by Howard [25]   At the time of the rupture the patient often feels something "give" beneath the upper sternum   Very soon afterward, he complains of epigastric pain and dyspnea The occurrence of this syndrome as the result of physical strain

makes it an important one to differentiate from angina The history of onset, the loud aortic regurgitant murmur, and the rather unexpected, fairly rapidly progressing cardiac decompensation are points of importance in the diagnosis Howard states that such patients may subsequently develop the typical anginal syndrome

Gastric disturbances of various kinds frequently give rise to substernal pain It is well known that the pain of a duodenal ulcer may be beneath the upper third of the sternum In one of our patients, smoking produces a dull, substernal ache probably of gastric origin, since it is relieved by food and soda This type of pain has been attributed to hyperacidity

Gastric distention may both simulate and help to produce anginal pain It may be the mechanism which causes angina pectoris after a heavy meal Verdon[19] has advocated and practiced the passing of a stomach tube during the attack to relieve this distention and reports good results We have been particularly interested in this phase of angina pectoris since the appearance of a patient in our clinic with the following picture Age thirty six years, no evidence of syphilis, onset of anginal attacks one month after a left lower lobe pneumonia four years ago, x ray evidence of an elevated left diaphragm adherent quite high to the lateral chest wall This patient's pain comes on as a result of exertion, but is infrequent except after a meal We suspect that the elevated left diaphragm when pushed still higher by a distended stomach is a very important factor in this patient's angina pectoris, in that it might tend to swing the body of the heart to the left Since the aorta is held fairly firmly in position this displacement of the heart might cause a compression of the left coronary artery near its orifice at the junction of the heart with the aorta It seems that this may be an explanation of the way in which gastric distention predisposes to the occurrence of an anginal attack, and it may throw some light on the mechanism of relief by belching, so often recounted by patients

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simulate that of angina pectoris   The possibility that the esophagus can give rise to substernal pain on exertion after meals has been impressed upon us recently   A patient complaining of this symptomatology was being examined fluoroscopically during an attack of mild lower sternal pain   A glass of bismuth given to test his swallowing function relieved his pain, and this procedure has relieved him ever since   We are inclined to attribute his "angina pectoris" to an esophagitis

A diphragmatic hernia in one of our old fibrillating cardio-sclerotics is probably the cause of a pain in the second left interspace which we suspected at one time to be anginal   The pain occurred after exertion, lasted a long time, and was particularly frequent and prolonged at night

A boy, aged twenty-one, a student in the University of Pennsylvania, preparing for his final examinations, came to our clinic a short time ago   He complained of pain on exertion over the body of the heart and in the left pectoral region   The pain was of a fairly definite paroxysmal nature   It occurred when he walked to class, and was relieved when he stopped to rest   It differed somewhat in intensity and character from the usual submammary ache or knife-like pain of an overworked, over-nicotinized, under-rested, worried, examination-taking student   Additional questioning brought out the facts that the onset was probably related to a wrestling match he had indulged in a week before, there had been no dyspnea nor cough, he had noticed, on running, a sensation as though his heart were "flopping around loose" inside of him, and five days before, his room-mate, while across the room, had heard his heart beating   His heart sounds, which were strong and easily audible in the erect posture with the stethoscope, could not be heard when he assumed the recumbent position

The physical signs suggested, and an x-ray confirmed the diagnosis of a partial pneumothorax, with about 200 c c of air pocketed around the apex of the left lung   The audibility of his heart sounds across the room we believe to have been due to the so-called "pericardial knock"[27]   However, we were unable to demonstrate this sign to our satisfaction at the time

of examination, although we listened for it in the various positions, and respiratory phases

A lesion in the spine, neck, lung, mediastinum, esophagus, stomach, or gall bladder may produce pain in the precordial region, but we must not forget the type of case, illustrated by a man in our wards last year. He complained of severe paroxysmal substernal pain. He was a minister of the evangelistic type, and the likelihood of such an occupation resulting in angina pectoris, together with the typical symptoms and the apparent pain he suffered, made us accept the above diagnosis for some time. Later developments, when a less respectful intern came on the ward, proved the man to be probably a malingerer in quest of morphin. His attacks subsided particularly rapidly when a rather ungentlemanly Irishman in the next bed threatened him with bodily injury if he should again disturb his night's rest. On looking back on the case, we should have been warned by this man's groans and general attitude during the attack. He was a little too noisy and was not sufficiently immobilized by the pain.

Following out the line of thought suggested by the tracings of Bousfield[11] and Feil and Siegel[12] we are beginning to believe that the electrocardiograph may be of value in the differential diagnosis of precordial pain. The majority of true anginal attacks which we have studied so far have been accompanied by electrocardiographic changes other than those attributable to the alterations in rate. Therefore, the occurrence of such changes during precordial or substernal pain of doubtful origin, has been of some aid to us in arriving at a diagnosis. The absence of such changes cannot be considered of much value in this connection, but at least one derives some moral support from it for a negative diagnosis. Unfortunately, the value of this method is limited to those patients who can be studied during an attack.

PROGNOSIS

There is no condition in which prognosis is more hazardous than in angina pectoris. Physical examination of the heart and blood-vessels may be entirely negative, the blood pressure

normal, Roentgen-ray examination reveal a heart of normal size
and shape, and the electrocardiogram show no evidence of
myocardial derangement, nevertheless, the patient may die sud-
denly within a short time   Such an event is admittedly excep
tional, but it occurs often enough so that one is never justified
in offering a completely favorable prognosis to the physician or
family of a patient who has suffered an undoubted attack of
angina pectoris

Despite occasional unexpected deaths the prognosis bears
relationship to the degree of damage involving the cardio-
vascular apparatus, to whether or not the impairments are
actively progressing or practically stationary, and also to the
frequence and severity of anginal attacks, the regularity with
which they follow exertion, and the amount of exertion necessary
to bring them on

From the point of view of prognosis, electrocardiography is
one of the most valuable methods of study available at present
Often it is the only examination that yields evidence of impair-
ment of the myocardium   Every patient, therefore, deserves
careful electrocardiographic study   The value of repeated trac-
ings in following the progress of heart disease has not been as
generally realized as it might be

Probably the reason why some patients, whose outlook
would seem to be bad, do so much better than we think they
will, is because the rate of deterioration of their hearts is much
slower than that which we expect to find

TREATMENT

The management of a case of angina pectoris is usually no
simple matter   If one employs only rest and nitrites he is bound
to share the almost universal pessimism regarding what can be
done for the sufferer with anginal attacks

One can scarcely overemphasize the importance of establish
ing a proper mental attitude in the patient   The nervous
apprehensive individual with the shadow of impending death
constantly darkening his outlook must be educated to a hopeful
point of view   In this respect one finds that his most difficult

patients are likely to be physicians One must be inflexibly optimistic and be prepared to support his position by citing favorable cases On the other hand some patients particularly those who have only mild attacks of pain, may be careless of our warnings In order to obtain their co-operation it may become necessary to stress the more serious features of their impairment. The management of each case from the point of view of psychotherapy, will vary No error is more unpardonable, however than to add to the fear of an already apprehensive sufferer It is necessary to gain the confidence of a patient so that he will discuss the state of his business and family affairs Sometimes an apparently calm individual will be found to be cultivating a placid exterior merely to mask the seething fires within Often a frank discussion will pave the way for the adjustment of his difficulties

The importance of proper rest and the avoidance of strain, both physical and mental, can scarcely be overemphasized Rest in individual cases may vary from a slight restriction of the daily routine to six weeks in bed followed by very gradual resumption of activity, depending on the severity of the case The guiding principle which Mackenzie has so strongly emphasized is to keep activity below the level at which attacks are excited

No possible point in treatment should be overlooked Everyone understands the importance of careful regulation of diet, the care of the gastro-intestinal tract and the interdiction or strict limitation of tobacco and alcohol But rarer factors in the production of angina, such as anemia or slight hyperthyroidism, may be readily overlooked

Invariably the question arises as to what to do about focal infections In our experience the removal of doubtful or slight focal infections has not yielded impressive results Undoubtedly, however, the eradication of extensive foci whether located at the roots of teeth, in the tonsils, sinuses, gall bladder, or prostate, may be well worth while What the result will be is always a gamble, and the risk of a tonsillectomy or a cholecystectomy even under local anesthesia has to be carefully weighed against the probability of bringing about improvement

Except for the relief of pain during the attack by nitrites, carminatives, or if necessary, morphin, medicinal treatment should be considered last   Sedatives are often of value, particularly fractional doses of phenobarbital in cases with hypertension   Sodium sulphocyanate is also a remedy worthy of trial in the nervous hypertensive patient   Theobromin and theophyllin ethylendiamin are of real value in some cases, probably due to their ability to dilate coronary blood-vessels   Digitalis is frequently used, but is seldom of value   It does, however, often relieve the more continuous types of pain found in association with heart-failure, probably by virtue of helping to restore compensation   Iodids are seldom helpful, but it is justifiable to try them even in non-syphilitic cases

Recently surgical methods of treatment and attempts to inject paravertebral ganglia have excited a great deal of interest These procedures are still in the experimental stage   At the present time it is not justifiable to submit patients to operation unless pain is so severe and uncontrollable that life becomes a burden, and one must realize that in these cases the advanced circulatory disease usually present makes surgical intervention extremely hazardous   Injection of ganglia is not so serious and the selection of cases need not be so rigid   The attempts to improve our therapeutic armamentarium along these lines deserve the greatest encouragement and we should not allow ourselves to become prejudiced by unfavorable results at this stage of the work

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TYPHOID INFECTION IN A PATIENT WITH MITRAL STENOSIS A DISCUSSION OF SOME OF THE CARDIAC COMPLICATIONS IN TYPHOID FEVER

Although typhoid fever is no longer the problem that it once was, it is far from being extinct in this country Epidemic outbreaks of major proportions still occur (Montreal, 1927) and each summer and autumn see enough cases in most of our medical wards to furnish material for an exposition of this disease to our students We propose to discuss briefly some of the cardiac complications in typhoid infection and to present a case possessing certain features of unusual interest in this connection.

It is, of course, obvious that practically all acute infections are capable of causing damage to the heart, however in certain respects, the cardiovascular picture in typhoid fever differs from that in other acute infectious diseases

The composite cardiovascular picture of typhoid fever may be summarized as follows The pulse rate is increased, but usually not in proportion to the fever, especially in the earlier stages of the disease, even with high fever the pulse rate may not be greatly increased (Osler[1] reports a pulse rate of over 140 in only 15 per cent of a series of cases observed by him) Dicrotism is said to be common The pulse usually remains of good quality throughout the course of the infection, but in some cases may become weak and thready at times imperceptible. The heart sounds, as a rule, are changed, the first sound often becoming feeble and impure and the second sound at the mitral area progressively more accentuated as the disease progresses

Systolic murmurs, usually soft and heard more often at the apex, may develop and are due probably to relative cardiac dilatation The blood-pressure usually falls gradually until the end of the febrile period, it slowly rises during convalescence Various types of arhythmia may occur and there is often a tendency toward embryocardia Bradycardia is common during convalescence There is a loss of tone in the peripheral vessels and a capillary pulse has been described The myocardium is often the seat of toxic degenerative changes, circulatory collapse, with rapid, feeble pulse, cardiac dilatation, cyanosis, and sudden fall in blood-pressure may occur during the height of the infection There are no pathologic changes in the myocardium peculiar to typhoid fever Pericarditis and endocarditis are extremely rare (the latter will be further discussed below)

The following case is of interest for several reasons (1) Because the clinical picture presented at first required careful analysis for identification, particularly because of the possible presence of bacterial endocarditis, (2) the response of a heart previously injured and suffering a mitral stenosis to a severe infection with Bacillus typhosus, (3) the association of a violent psychosis, which has continued to the present It affords an opportunity to discuss the general question, comparatively neglected in recent American literature, of cardiac complications in typhoid fever

The patient, Mrs Sarah K, a Russian-Jewish female of thirty-two years was referred to the service of Dr Alfred Stengel by Dr M Jacob on March 8, 1929 At the time of admission, she had been ill about twenty days, the onset having been gradual There had apparently been fever of varying degree, general malaise, abdominal distress, and a tendency toward constipation The stools were said to have been foul and at times had contained dark blood There had been several nose bleeds, the patient had been nervous and agitated, and had rested but little Her physician had noted several spots on the abdomen which he considered to be rose spots The spleen was reported enlarged and the Widal reaction was positive. The patient had not been out of the city within the recent past

nor had she partaken of any food or drink which could be considered suspicious   There was no history of any other acute infectious disease within her family   The past medical history as obtained from her husband contained no items of significance beyond an occasional mild sore throat, together with the usual minor diseases of childhood   There was no history of rheumatic fever or chorea   The menstrual history was essentially normal except for two miscarriages   The patient had been born in Russia but had lived in Philadelphia for about fifteen years

On examination at the time of admission she appeared somewhat listless, but quite wide awake and entirely co-operative   The skin was dry and a little glazed and shiny to the right of the sternum   The eyes were a little prominent, the pupils in mid position, and reacted normally   The tongue was dry and furred, the breath heavy and offensive and sordes were present around the lips   The pharynx was a little red and contained much thick ropy mucus   The tonsils did not appear enlarged or obviously infected   There was no cervical adenopathy or thyroid enlargement   Examination of the lungs was essentially negative   The heart was not enlarged to percussion   The rhythm was normal, but the rate was markedly accelerated (140), and the radial pulse was thready, quick, and easily compressible.   There was a tendency toward fetal spacing of sounds which made it difficult to distinguish the first from the second sound and consequently rather difficult to time the murmurs which were heard   A definite presystolic murmur of crescendo type was heard at the apex, it was not transmitted   The first sound at the apex was markedly accentuated and there was later, after the heart action had quieted somewhat, a presystolic thrill palpable at the apex   Over the cardiac base, a soft systolic murmur transmitted into the vessels of the neck was audible   The blood pressure on admission was 120/78   The abdomen was slightly distended and peristalsis was diminished   Over the upper abdomen were a few suggestive rosaceous spots   The edges of the liver and the right kidney were easily felt, but neither was tender   The edge of the spleen was defi-nitely palpable but seemed soft and easily slipped away from

the examining finger-tips The patient was menstruating, two weeks early, at the time of admission

The urine contained nothing of importance beyond a trace of albumin and a moderate number of leukocytes The blood count showed R B C, 3,300,000, Hb, 47 per cent, W B C, 11,400, with a slight excess of neutrophils in the differential At the time of admission it was thought that the two diagnoses to be considered principally were first, typhoid fever occurring in a patient with old mitral stenosis, and second, subacute or acute bacterial endocarditis The Widal test was repeated and was found positive in high dilution On the fourth day after admission, the temperature dropped abruptly to normal, but the pulse remained rapid, as it did during the patient's entire stay in the hospital A moderate leukocytosis up to 12,400 likewise persisted No petechiæ were observed at any time, but the spleen remained palpable for about ten days The first blood-culture taken immediately on admission remained sterile, but B typhosus was recovered from a second blood-culture made two weeks after admission as well as from the urine No typhoid organisms were ever recovered from the stools After the first abrupt subsidence of fever, the temperature gradually rose again and by the fourteenth day (approximately the thirty-fourth day of illness) had reached 104° F Thereafter it gradually subsided to a range between 98° and 100° F, which level was maintained at the time of discharge The pulse-rate, however, continued markedly accelerated and at the time that the recrudescence of fever had reached its height, the pulse-rate was 160 The cardiac rhythm remained normal and the murmurs heard on admission did not change in character At no time was any cardiac enlargement demonstrable by percussion Twelve days after admission, it was noted that the patient was slightly irrational and jocose She continued reasonably co-operative, however, until three days later, when she developed a violent antipathy toward her nurse, insisting that the nurse was attempting to poison her It became necessary to change nurses, but the patient s psychosis progressively increased in the severity of its manifestations and on the nine-

teenth day she refused all food by mouth It became necessary to institute nasal tube feedings which had to be continued until discharge The patient became maniacal, shouting and cursing loudly, jabbering a jargon Yiddish and making constant efforts to free herself from restraint She was incontinent of urine and feces, would withdraw her nasal tube whenever possible and on numerous occasions spat upon and struck her attendants These manifestations continued almost unchanged and on May 14, 1929, after three negative cultures had been obtained from stools and urine, she was transferred to her home

After removal to her home, she continued to run occasional mild fever up to 99³⁰ F, the pulse-rate and cardiac findings remained unchanged The psychosis persisted and a week after removal to her home it became necessary to commit her to a hospital for mental diseases, where she is now confined

In reviewing the details of this case several possibilities present themselves In the first place, it is possible that the murmurs heard at the cardiac apex were the result of a mitral endocarditis which developed during the course of the typhoid infection and which might have been caused either by the B typhosus or by some associated organism, such as a streptococcus or staphylococcus This possibility, while indeed remote, deserves some consideration, as a further discussion of so called "typhoid endocarditis" will show

Second, it is possible that this patient may have exhibited a rare coincidental infection with B typhosus and one of the varieties of streptococcus causing subacute or acute infective endocarditis Our failure to recover any organism save the typhoid bacillus from the blood-stream and the subsequent clinical course, with defervescence, argue strongly against the likelihood of this

The third possibility, and the one which appears most likely, is that there was present a mitral stenosis resulting from an old mitral endocarditis (probably of rheumatic origin) and that the rather unusual cardiovascular picture seen in this case was the result of the response of an already damaged heart to a severe generalized infection Under these circumstances, it is

not surprising that a tachycardia so marked and so constant should have been present It is true that no history of tonsillitis, chorea, or rheumatic fever could be elicited from the patient or her family, but the occasional discovery of such "silent" mitral stenoses is not rare It must, however, be remembered that the case is not yet a closed one Future developments may cause us to alter our opinion, but at present the above combination of circumstances seems nearest the truth

It is unnecessary to point out that typhoid fever, like other acute infectious diseases, may cause sufficient damage to the myocardium to prove an important factor in the subsequent development of chronic myocardial disease, nevertheless, but little attention appears to have been paid to this subject in American and English literature in recent years, perhaps because typhoid infection is considered more or less a closed chapter The French have been the principal contributors in this field, although Thayer's[2] study of the late effects of typhoid fever in the cardiovascular system, in 1904, is important Thayer examined a series of 183 patients who had had typhoid fever previously, at intervals varying from one month to thirteen years after the infection He was able to show

1 A distinct tendency toward elevation of the systolic blood-pressure, as compared with a group of normal controls

2 An apparent increase in evidence of peripheral vascular sclerosis (palpable radial arteries), as compared with a group of normals of similar age (ten to fifty years)

3 A slight increase in cardiac dimension to the left

4 Ten instances (5 4 per cent) in which definite cardiovascular lesions developed in the absence of any other generally recognized etiologic factors—there were 7 cases of cardiac hypertrophy with mitral insufficiency, 2 of aortic insufficiency, and 1 of marked arteriosclerosis with hypertension occurring in a young man Thayer mentions the relation of acute infectious diseases to arteriosclerotic processes in general and points out the importance of typhoid fever in this respect

Clerk and Robert Levy[3] have studied the electrocardiographic changes during typhoid fever In 3 cases of moderate severity

definite changes were found, the T wave being inverted or flattened, in 5 cases of severe infection the T wave was negative or diphasic, in 3 instances during convalescence the T wave again became positive and acquired its normal height   There was no specific electrocardiographic picture described for typhoid fever

DeBrun[4] has reviewed the subject of myocardial disease and disturbances of rhythm during typhoid fever and Etienne[5] has pointed out that such myocardial disease may reveal itself long after the acute infection by sudden cardiac failure under strain.

Endocarditis caused by B typhosus or other organisms during the course of typhoid fever is exceedingly rare, indeed, its occurrence is doubted by some writers   Thayer[2] mentions 3 in 100 necropsies on typhoid patients at the Johns Hopkins Hospital and 11 in 2000 Munich necropsies   Hare and Beardsley[5] state that the usual cause of such endocarditis is a "mixed infection," but refer to the recovery of B typhosus from the valvular endocardium   Many of the earlier cases are to be accepted with reservations, but such reports as those of Leuvrierre, Deschamps and Bernard,[7] who describe a mural endocarditis near the apex with a thrombus or vegetation from which B typhosus were recovered, and Minet and Legrand,[8] leave little doubt that endocarditis can be produced by the typhoid bacillus There is apparently no predilection for any particular valve Infective emboli may be dislodged from the endocardial lesion and cause vascular obstruction in various parts of the body, particularly the extremities, spleen, and brain   Cardiac signs may not be found even in the presence of an acute endocarditis and the occurrence of systolic murmurs is of little diagnostic value in this respect during the acute stage since such murmurs often appear as a result of relative dilatation   The development of a diastolic or presystolic murmur during the course of a typhoid infection would, of course, lead to strong suspicion that an endocarditis has developed or that a previously silent endocardial lesion has manifested itself by a murmur under the strain of the acute infection

Of particular interest are those cases described by Thayer[2] in which definite evidence of aortic insufficiency, mitral insufficiency, and mitral stenosis with insufficiency, respectively, appeared shortly after typhoid fever, in the absence of any recognizable etiologic factor It is certainly difficult to escape the conclusion that the typhoid infection either actually produced endocardial damage in these cases or brought out a latent murmur, the result of an old endocardial lesion The absence of any history of any other etiologic agent in these cases would argue against the latter possibility

Vasilesco et al [9] report an instance of typhoid fever followed by a persistent sepsis for sixteen months, with the development of an ulcerative aortitis and an aortic aneurysm which ruptured—no statement is made concerning the identity of the causative agent

The occurrence of typhoid fever in an individual with an old endocardial lesion must of necessity be comparatively rare, when such a coincidence is encountered particularly careful study is necessary for diagnosis and an unusual cardiac response to the infection may be seen

SUMMARY

1 A case of typhoid infection occurring in a patient with probable old mitral stenosis is reported and the clinical picture and problem of diagnosis are discussed

2 Typhoid fever may be an important factor in producing permanent myocardial damage, and in contributing toward the development of arteriosclerotic processes in general

3 Endocarditis caused by Bacillus typhosus is rare, but does occur

4 Typhoid infection occurring in an individual with an old endocarditis may excite an unusual cardiac response, particularly a tachycardia beyond the usual range

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CLINIC OF DR JAMES E COTTRELL

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LIPOID NEPHROSIS, WITH ESPECIAL REFERENCE TO MIXED CASES

The syndrome commonly known as lipoid nephrosis is defined by Elwyn in the following terms "A disease characterized by an insidious onset, a chronic course, edema, oliguria, albuminuria changes in the protein and lipoids of the blood and the deposit of lipoids in the kidney, it occurs alone or in combination with diffuse glomerulonephritis or with amyloid degeneration of the kidneys " Its clinical features were adumbrated in the classical descriptions of chronic parenchymatous nephritis Friedrich Müller in 1905 coined the term "nephrosis" to distinguish those affections of the kidney which are characterized primarily by degenerative changes, especially in the tubules, from those which are primarily inflammatory or due to vascular sclerosis In 1913 Munk, selecting from the confused group of so-called nephroses those cases which exhibited the main symptoms named in the above definition, and finding double refractive lipoids in the urine and in the cells of the kidney tubules, applied to them the name lipoid nephrosis Volhard and Fahr, about the same time, described similar cases under the name of "genuine" or "chronic" nephrosis In this country, Epstein studied the subject so extensively that his name is often attached to the syndrome, he set forth the idea that the condition is a perversion of general metabolism in which the renal features present only one aspect, and he introduced the high protein diet in treatment Eppinger, on empiric grounds, used thyroid gland in treatment before studies showed that the basal metabolic rate is often diminished

Elwyn devotes a chapter of his monograph on kidney disease to lipoid nephrosis Many case reports and many discussions are to be found in the literature, but the real nature of the condition has not yet been satisfactorily explained

The patient whose case is the principal subject of my discussion is a married white woman, thirty-seven years of age Her chief complaint is swelling of the ankles In July, 1927 when her youngest child was eleven months old, she noticed slight swelling of the left ankle and leg in the evenings Gradually progressing, the swelling involved the right ankle for the first time in November, 1928 By March 1, 1929 both ankles and legs were swollen all of the time No swelling of any other part of her body had been noticed Since the summer of 1928 exertion, such as running upstairs, has caused dyspnea, but there has been no progressive increase in this symptom For some months she has had palpitation when lying down, vertigo on getting out of bed suddenly in the morning, and occasional vague, dull, non-radiating precordial pain, none of these is seriously annoying She has no polyuria nor nocturia She occasionally has "bilious attacks," precipitated by over-eating, and marked by weakness, nausea, vomiting, and headache, there are no other gastro-intestinal complaints She thinks she is rather sensitive to cold Her maximum weight was 143 pounds in July, 1927, when admitted to the hospital she weighed 129 pounds

She had scarlatina at the age of five with "dropsy," but was alleged to have made a complete recovery At eleven, she had typhoid fever and was confined to bed for three months She has two children, one born in 1916 and the other in 1926, in the second and third months of the first pregnancy she suffered from hyperemesis, but had no late toxemia In July 1928 she had grippe and stayed in bed two days In October, 1928 she had a curettage and a cauterization of the cervix for cervicitis Her family history is irrelevant

For three months before admission to the hospital on March 18, 1929 she had been taking a diet greatly restricted in protein and in salt, but had shown no improvement At the time of

admission the following were the noteworthy features in the physical examination   slight undernutrition, a rather pasty pallor, slightly unequal but normally reactive pupils, normal ocular fundi, small, imbedded cryptic tonsils, evidently infected, absence of all upper teeth, which were replaced by a plate, absence of many teeth from the lower jaw, a soft systolic apical murmur transmitted toward the axilla, but no cardiac enlargement, blood pressure of 138/85, marked edema of both legs as far up as the knees

The urine has consistently contained a "cloud" of albumin (quantitatively 1 5 to 3 gm per liter) and on a few occasions a number of hyaline and granular casts   A very few doubly refractile lipoid granules were found in the urinary sediment on two occasions   Phenolsulphonephthalein elimination, after intravenous injection of the dye, is 65 per cent. in two hours   In the urine concentration test, the specific gravity has ranged from 1 015 to 1 024, but the volume of the night urine approaches or exceeds the volume of the day urine   The van Slyke urea clearance test and the King urea tolerance test have both shown definite impairment of power to excrete urea

The blood-urea nitrogen has ranged from 10 to 18 mg per 100 c.c., the blood uric acid is 3 3 mg per 100 c c , the blood cholesterol, in two determinations, was 333 and 376 mg per 100 c.c.   The hemoglobin has been 82 to 87 per cent (Sahli), the erythrocytes 4 3 and 4 4 millions, the leukocytes 7000 and 8000, and the differential count normal   The blood Wassermann is negative

At the first determination the total serum protein was 3 64 gm per cent., albumin 1 46 gm per cent., globulin 2 16 gm per cent.   The patient's daily diet was arranged to contain 120 gm. of protein, 60 gm of fat, and 175 gm of carbohydrates   About ten days later the serum albumin was 1 53 gm per cent , and the globulin 3.54 gm per cent   A transfusion of 500 c.c. of citrated blood was given her in an effort to increase the protein content of her blood, we do not know the effect of this for a subsequent determination has not yet been made.   The rate of sedimentation of the erythrocytes is markedly increased,

when plotted according to the method of Cutler, the curve is of the vertical type which accompanies many pathologic conditions   The basal metabolic rate is +7 per cent , nevertheless she has been receiving 3 grains of dried thyroid gland per day

A tonsillectomy was done without serious reaction   A three-day course of theocin produced a fairly marked diuresis   Whether because of the high protein diet, the dried thyroid, or the theocin, the patient's edema virtually disappeared, she felt much better and she has been allowed up and about the ward   Although there has been a slight recurrence of the edema in the past few days, she is now ready for discharge

For comparison, I wish to present brief histories of two other patients whom I have had an opportunity to observe in the Episcopal Hospital within the past year

A private patient, Mr D , a married white man of forty-five years, was admitted on August 6, 1928   In subjectively perfect health until two months before, he had since suffered from nausea, vomiting, and weakness, his feet had been swollen since the onset of his symptoms   There were no other complaints except a little vertigo and a tendency to constipation   He had had nocturia, once per night, for a long time   His urine was said to have boiled solid with albumin on a recent occasion He had been on a low-protein, low-salt diet since onset   He had had a chronic discharge from one ear since early manhood In 1926 he had a chancre, he received extensive antiluetic treatment from his family physician, including large doses of mercuric chlorid by mouth (1/10 of a grain t i d for several months)

When admitted, there was slight puffiness of the eyelids and edema of both lower extremities extending to the buttocks The heart was slightly enlarged to the left and the blood-pressure was 155/106   The retinal vessels showed a moderate increase of the light reflex, but no marked sclerosis, there were no retinal hemorrhages nor exudates

For some time after admission he was greatly troubled by nausea and vomiting, so that he was unable to take food   The previously noted edema increased, and involved the scrotum,

signs of a right pleural effusion appeared The urine always contained a "cloud" or a "heavy cloud" of albumin and numbers of hyaline and granular casts, the specific gravity ranged from 1 006 to 1 035 The phenolsulphonephthalein excretion was 25 per cent in two hours The blood urea nitrogen was 24 6 mg per 100 c.c. on admission, and it rose to 38 2 mg per 100 c c. during the time in which nausea and vomiting were most marked and the edema was increasing, just before the patient's discharge from the hospital it had fallen to 16 6 mg per 100 c c in spite of the higher protein intake The blood creatinin ranged between 1 6 and 2 6 mg per 100 c c , the uric acid was 4 1 and 5 mg per 100 c.c , the cholesterol 340 mg per 100 c c , and the plasma CO_2 content 65 5 volumes per cent On three determinations the serum albumin was 1 0, 1 3, and 1 0 gm per cent , and the globulin 2 4, 2 3, and 4 2 gm per cent The basal metabolic rate, on two successive days was −11 per cent and −12 per cent The blood-count was not significant except that once the leukocytes were 14,800 The blood Wassermann was negative When the pleural effusion was aspirated, half a liter of slightly milky fluid was obtained, its specific gravity was 1.003, and its cholesterol content 70 mg per 100 c.c

The patient was given a diet fairly rich in protein but not definitely measured, no thyroid preparations nor diuretics were used His nausea subsided, his edema rapidly diminished, and the urinary output increased and he felt greatly improved At the time of discharge, his blood pressure was 155/98 After some weeks of rest at his home, he was able to return to his occupation When last heard of, he was proceeding comfortably, with little or no edema, but with persistent albuminuria, cylindruria and hypertension

The remaining patient, Mrs T , was a married white woman of thirty-six years, she was admitted to the Episcopal Hospital on the service of Dr John M Carson on October 24, 1928 Her chief complaints were shortness of breath and swelling of the legs and abdomen A month previously had "caught a severe cold in her chest", soon afterward she developed, successively, swelling of the left leg, dyspnea, and swelling of the right leg

A physician examined her urine and told her she had Bright's disease   Her abdomen began to enlarge, and she was uncomfortable, dyspneic, and "cold all over her body", her lips and finger-nails were blue   Her urinary output diminished to as little as half a pint a day   During the week before admission, fluid began to ooze first from the left flank and then from the right   She had no serious previous illnesses, but had had a "bronchial cough" as long as she could remember and nocturia for several years   She had two children, aged five and two-and-one-half years

She appeared very ill, and was orthopneic, pallid, and drowsy She exhibited a most remarkable degree of edema   The legs were huge and cylindrical, she could scarcely move them because of their weight   The abdomen was enormously swollen, the flanks bulging far out   The skin of the lower abdominal wall showed many tortuous "channels" extending up toward the thorax, broader at their lower ends, slightly raised, pale, almost translucent   These were at first thought to be dilated lymphatic vessels, but were probably extremely edematous striæ of former pregnancies   Fluid oozed freely from the skin of both flanks, saturating dressings quickly and keeping the bed wet   The trunk was edematous as far up as the arm-pits and the arms slightly so, the face was not puffy   The eye-grounds were normal

Her urine always contained a "heavy cloud" of albumin, and hyaline and granular casts, the specific gravity was from 1 029 to 1 032, the usual twenty-four-hour volume was about 500 c.c The phenolsulphonephthalein excretion was 45 per cent in two hours   The hemoglobin was 60 per cent (Dare), the erythrocytes 3 5 millions, the leukocytes 12,800, and the differential count normal   The blood-urea nitrogen was 11 mg per 100 c.c., the cholesterol 360 mg per 100 c c , the serum albumin 2 1 gm per cent , the globulin 2 36 gm per cent   The blood Wassermann was negative

Eight Southey tubes were inserted in the patient's legs and thighs, the drainage in about twenty-four hours amounted to 6650 c c   Under theocin, the urinary output reached a max

mum of 1250 c.c The oozing of fluid from the flanks ceased, and the edema of the legs diminished to a slight puffiness Her diet was arranged to contain 100 gm of protein, 50 gm of fat, and 50 gm of carbohydrate per day In a few days the edema recurred, diarrhea developed (probably from edema of the intestine), the patient grew rapidly weaker and soon died, apparently from exhaustion Necropsy permission was refused

These cases exemplify the cardinal features of lipoid nephrosis, together with complicating factors in at least two of them To go into any full explanation of the individual features would require too much time and lead us too far into speculation

The generally accepted explanation of the deceptive pallor, which causes these patients to appear more anemic than they actually are, is that it is due to constriction of surface capillaries Such constriction would appear to be an effort to minimize the edema by lessening transudation through the capillary walls There are three obvious possibilities to aid in explaining the production of the edema First, the alterations in the composition of the blood, second, some alteration in the permeability of the capillaries, third, some change in the protoplasmic chemical composition or reactions of the tissue cells, so that they absorb more fluid. Such changes in the capillaries and in the tissue cells might be due to the unknown toxin, or unknown perversion of cellular metabolism, which underlies the condition The edema fluid itself is dissimilar in composition to that found in acute diffuse nephritis or in cardiac decompensation, the protein content, and according to some investigators the chlorid content also, is lower in the edema fluid of nephrosis In regard to the albuminuria, two principal explanations appear, each more or less correlated with a particular conception of the pathogenesis of the condition In the urine, albumin vastly predominates over globulin, it may be assumed that the hypothetical causative toxin (which attacks most or all of the body cells in varying manners and degrees) injures the cells of the kidney tubules and of the glomerular capillary tufts so as to make them more permeable to protein, and especially to albumin because its molecules are smaller than those of globulin On the contrary,

others assume a qualitative change of unknown nature in the albumin, which makes it unfit to subserve its normal purposes in the body, it is therefore eliminated by the kidney, as though it were a foreign protein   Such a change would imply a general perversion of protein metabolism, it is with this in mind that Epstein applies the term "diabetes albuminuricus" to the syndrome

The loss of albumin in the urine, whatever its explanation, accounts for the lower amount of albumin in the blood   The "normal" amounts of serum albumin and serum globulin are stated differently by various writers, a consensus of opinion is that the albumin should be between 3 5 and 5 5 gm per cent , and the globulin between 1 5 and 3 5 gm per cent   In all three of our present cases the albumin is greatly decreased, the globulin either normal or slightly increased   In many of the reported cases the globulin is absolutely as well as relatively increased, Linder, Lundsgaard and van Slyke believe that this is because it is easier for the body to synthesize globulin than albumin   It seems possible that dietary restriction of protein which was practised in our first 2 cases, and which is so common if the situation is not completely studied, may contribute to the deficiency of blood protein   The increased cholesterol content of the blood has been believed to be due to an effort by the body to compensate for the decrease of protein, in our cases the cholesterol is well above the normal of 175 to 225 mg per 100 c c   The hypercholesterolemia and an increase in blood fibrinogen account for the speedy sedimentation of the erythrocytes

The lowered basal metabolic rate, which has been stressed in some writings, is not conspicuous here   It is evidently not an essential feature of the syndrome and may be more apparent than real   These patients are usually somewhat undernourished, which of itself decreases the metabolism   A degree of edema which would pass almost unnoticed may yet represent a considerable proportion of the patient's body weight, and thus constitute a source of error in the calculation

The etiology, in spite of all that has been written on the

subject, remains unsettled Epstein believes the condition to be a general metabolic disorder That, however, does not explain the cause, and it may be suspected, because the lowered metabolism is not noted in all cases and may be even spurious, that the metabolic aspect has been overemphasized Munk believed that syphilis is the most important cause A case has been reported in which carbon monoxid poisoning shortly before the onset of symptoms was believed to have been a causative factor In a recent case studied by Talley and Glenn, the patient was in the habit of taking enormous doses of phenol phthalein to relieve chronic constipation and this was suspected as the cause In our second case the history of large doses of mercury raised the question of kidney damage from that source The condition seems often to be associated with pregnancy When lipoid nephrosis occurs as a complication of chronic glomerular nephritis, the former is probably caused in some way by the latter, just what the determining factor is, we cannot say One may wonder, too, whether or not our low protein diets, prescribed with none too great discrimination in cases of nephritis, may aid in inducing the condition We may have been too strict in our limitation of protein intake

In treatment, the most important measure seems to be a diet rich in proteins and moderately restricted in fats The ostensible purpose of the high protein diet is to remedy the deficiency in blood protein, Elwyn believes, however, that any benefit produced is due to the specific dynamic action of protein in stimulating metabolism Desiccated thyroid in rather large doses, as recommended by Eppinger, sometimes seems to produce decided benefit As in two of our cases, xanthin diuretics often aid materially in reducing edema, as does also restriction of fluid and salt intake In some of the cases with glomerular nephritis and a tendency to azotemia, it may be a rather nice problem to balance the protein intake so as to supply enough to combat the nephrosis and yet not cause too much nitrogen retention That problem is one for individual solution in each case, depending on how the patient does best

The condition runs a chronic course and most cases, if not

all, eventually terminate fatally   The patients may die of the
underlying disease if any is present, for instance, chronic glom
erular nephritis, or of an intercurrent infection   An especial
tendency to pneumococcic infections has been described   The
cause of death in our third patient is obscure   On the other
hand, some patients, after improvement, may continue in com-
parative comfort for many years, but usually with residual
symptoms

Pure lipoid nephrosis, it is rather generally agreed, does
not cause "renal insufficiency" in the sense of progressive de-
terioration of the kidney's ability to perform its normal work
of excretion   But lipoid nephrosis is more often seen combined
with other types of renal disease, especially chronic glomerular
nephritis, than alone   Our first patient shows evidences of an
underlying glomerular nephritis in the beginning, loss of ability
to concentrate (increase in volume of night urine), and in im-
pairment of urea excretion   The second patient showed clearer
evidences in the nitrogen retention, hypertension, and impair-
ment of phenolsulphonephthalein elimination   Pure lipoid
nephrosis is undoubtedly a rare condition, but combined with
chronic glomerular nephritis it is probably more common than
has been supposed   I remember, as no doubt everyone of us
does, many pallid, edematous patients with hypertension and
azotemia, obviously suffering from chronic nephritis, with the
traditional superiority of hindsight, it now appears possible that
in some of those cases further study might have revealed the
presence of a complicating lipoid nephrosis   Every patient
presenting such a picture should have the benefit of complete
study, especially determination of the blood proteins and
cholesterol   Their chance is none too good at best, but they
must have whatever opportunity may be offered by treatment
aimed to combat a complicating nephrosis, should it be found,
as well as the underlying nephritis

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MONOCYTIC LEUKEMIA

WHEN we come to consider monocytic leukemia, we find that it is a rare condition and that little has been written concerning it in the English language Merklen and Wolf (1928) were able to collect 24 cases Mr B will give us the history of the case presented here

MR. B The patient is a woman, sixty two years of age She was admitted on March 6, 1929 to the service of Dr Arthur Newlin, who has kindly allowed the case to be presented She complains chiefly of general weakness This began in May 1928, and gradually has been increasing Aside from weakness she has no complaints of any definite sort, except a disturbing roaring sound in the head Recently, she has lost a few pounds in weight She has always been well except for frequent heavy colds.

DR. FARLEY The history is such as might be elicited in any progressive anemia What are the findings on physical examination?

MR B The skin is quite pale The general nutrition is good The mucous membranes especially show pallor There is no jaundice The teeth have a peculiar greenish tint The gums are spongy, but there is no spontaneous bleeding The tongue is dry and coated The tonsils grossly show no evidence of disease The thyroid is of normal contour There is no cervical adenopathy, in fact, none of the superficial lymph nodes can be felt There is no demonstrable pulmonary lesion The heart is normal in size. A soft systolic murmur is heard at the cardiac apex The abdomen is full and tympanitic The liver and spleen are not enlarged to percussion or palpation There is no tenderness or rigidity of the abdomen The peripheral reflexes are equal and of normal range There is no edema
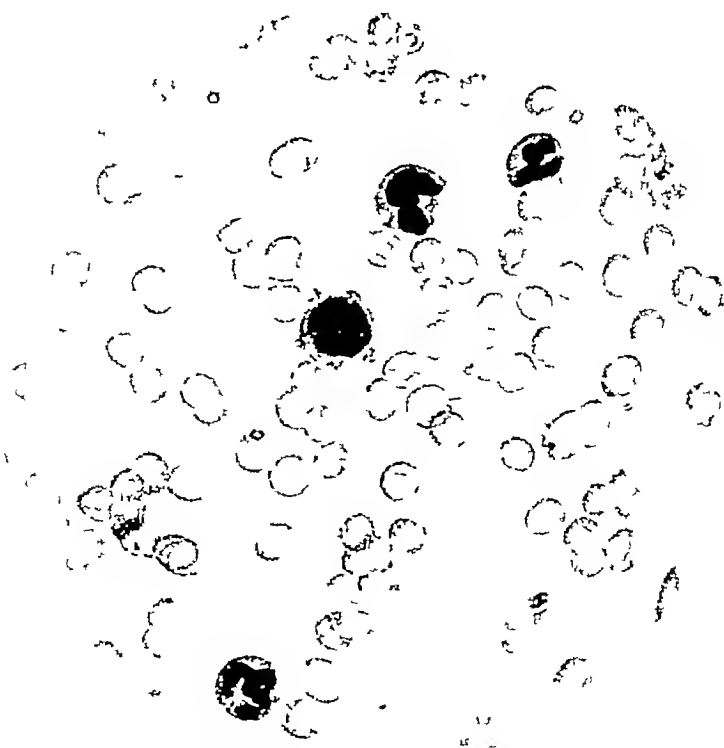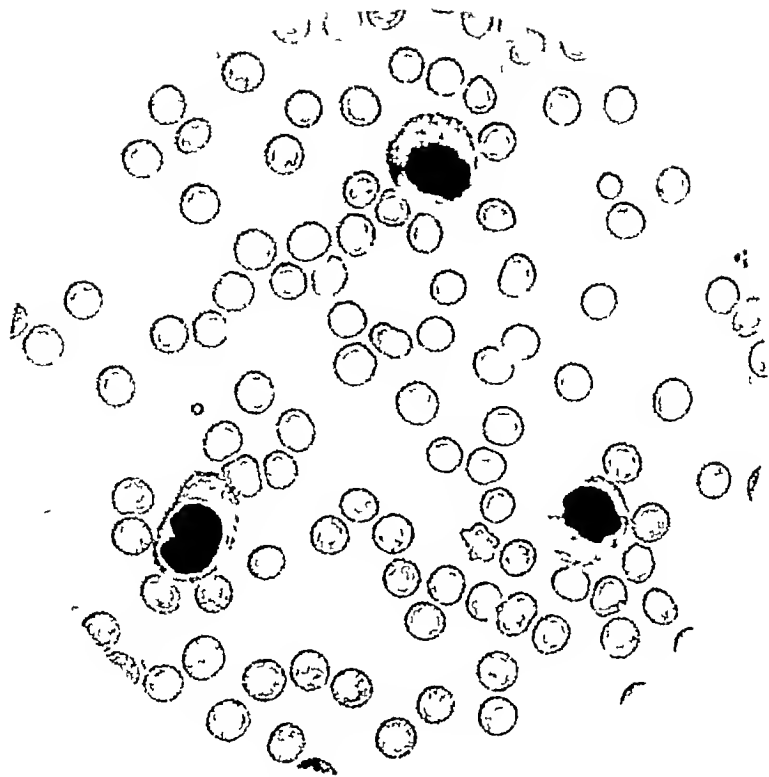
Figs 168 169 — Microphotograph of blood from case reported showing monocytes

Subsequent Course—The patient had a constantly elevated temperature during the three weeks preceding her death She developed ulceration and sloughing about the teeth and pharynx

Reported by	Course	Platelets per c mm	Coag. time	Basoph.	Eosin.	Mono-cytes system	Polls lymph-ocytes	Leuco-cytes per c mm	Non-granu-lar lymph	Spleen enlarged	Lymph nodes enlarged	Liver enlarged	Age	Sex
1 Reschad & Schilling (1913)	Acute					78 5%	5 %	10 100 to 80,000	920 to 4 110	Yes	Yes	Yes	23	M
2 Hirst (1917)	Chronic					90%	5	82,000 to 31,300					49	M
3 Lion & Parnot 1927	Chronic	3%	0 9%		95 5%	3 3	3 5	101,600	2 500 to 3,300	Yes	Yes	Yes	57	F
4 Lion & Parnot 1927	Chronic	0.25%			98 2%	3 3	95,000	3 034	Yes	No	Yes	41	M
5 Lion & Parnot 1927	Chronic	0 1%	1%		98%	6	154,000	4,098	Yes	Yes	Yes	71	M
6 Morel Tapie and Bourbonnais (1913)	Chronic	1%	5		89%	2 7%	370,000	2 800	Yes	Yes	Yes	60	M
7 Fontanel and Lilliecher (1925)	Chronic	0.5%	2 1%		95 1%	1%	39,750	1 900	Yes	Yes	Yes	9 M	M
8 Welll and Parvot (1925)	Chronic	3%	17%		61%	17%	15,000	2 500	Yes	Yes	Yes	60	M
9 Ewald O (19 3)	Acute	0.25%	4	0	94 7%	1%	13,000	1 850			Yes	53	M
10 Ewald Frohse and Rennic (1923)	Acute	0	Few		80%	1 5%	139,800	1 143			Yes	9 mos	M
11 Ewald Tobss and Rennig (19.3)	Acute		11 to 29%		42% 4 10 to 59%	4 10 to 50%	23 000 to 50,000	3 000	Yes	Yes	Yes	20	F
12 Marklee and Wolf (12.8)	Acute		14%		72 to 91%	7% 9%	30 500 to 35,000	3 100 to 1,750		Yes	Yes	30	M

Fig 170 —Summary of some reported cases of monocytic leukemia

Her teeth became loosened, and several were extracted to prevent her from swallowing them She was given several blood transfusions with resulting increase in red cells and hemoglobin,

but without any improvement in her general condition She died on April 21, 1929   She had no hemorrhages and did not develop purpuric eruptions

Average Urine Analysis —The specific gravity varied from 1 008 to 1 014, albumin, a trace to a heavy cloud   There were no red blood-cells, no pus, and no casts

x-Ray —The nasal accessory sinuses showed no evidence of lesions

The *blood Wassermann* test was negative

Blood Chemistry (3/9/29) —Sugar 103, urea nitrogen 35 2, creatinin 2 mg per cent

Van den Bergh Test (3/9/29) —Immediate direct, 1 unit per 100 c c

Blood Counts —

1929 Date.	% Hb	Per cm R. B C	Per cm. W B C.	% Poly	% Eo	% Baso	% Lym.	% Mono.
3/6	32	1,310,000	38,800	6	0	0	10	84
3/8	32	1,260,000	65,550	8	0	0	8	84
3/8			72,000					
3/10	38	1,920,000	64,650	8	0	0	7	85
3/11	38	1,710,000	50,000	6	0	0	8	86
3/12	38	1,480,000	63,500	7	0	0	9	84
3/13	45	2,330,000	29,000	9	0	0	3	88
3/14	38	1,980,000	43,500	3	0	0	2	95
3/15	38	2,180,000	46,500	3	0	0	7	90
3/16	51	2,540,000	37,000	4	0	0	5	91
3/17	51	2,350,000	36,000	7	0	0	4	89
3/18	51	2,330,000	23,000	6	0	0	7	87
3/18	58	2,900,000	36,000	8	0	0	5	87
3/19	58	2,510,000	17,500	19	0	0	7	74
3/20	58	2,770,000	12,500	21	0	0	12	66
3/21	64	3,350,000	13,850	16	0	0	6	78
3/22	64	3,070,000	14,650	20	0	0	6	74
3/23	58	2,340,000	11,450	18	0	0	7	75
3/24	58	3,080,000	10,300	24	0	0	6	70
3/25	58	2,910,000	14,550	30	0	0	20	50
3/26	58	2,440,000	21,000	31	0	0	12	57
3/27	71	3,000,000	27,100	26	0	0	6	68
3/28	71	3,560,000	26,150	27	0	0	12	61
3/29	71	3,100,000	27,700	32	0	0	14	54
3/30	64	3,290,000	23,500	34	0	0	10	56
3/31	77	3,530,000	25,150	43	0	0	11	46
4/1	77	3,460,000	27,100	44	0	0	4	52
4/2	71	2,960,000	25,250	26	0	0	11	63

Blood culture (3/25/29)—negative

Blood platelets (3/15/29)—155,000 per cm , reticulated red blood-cells 1 per cent

Necropsy was refused

DR. FARLEY The diagnosis of monocytic leukemia has been made in this case Upon what grounds does it rest?

MR B The diagnosis rests mainly on the study of the morphology of the mononuclear cells so abundant in the blood smears

DR. FARLEY Studies of that kind are hardly sufficient to make an absolute diagnosis of monocytic leukemia An opportunity to examine the spleen, liver, and bone-marrow is necessary Will you read the report on the morphologic studies of the blood smears?

MR. B On March 21, 1929, 500 cells were counted, showing monocytes, 80 6 per cent , lymphocytes, 3 8 per cent , adult neutrophils, 8.2 per cent , young neutrophils, 5 4 per cent , eosinophils, 0 4 per cent , basophils, 0 2 per cent , myelocytes, 0 4 per cent., neutrophilic megalopolycytes, 0 8 per cent , Türks cells, 0.2 per cent. The chromatin network of the nucleus of the monocytic cell was loosely woven and contained 1 to 3 nucleoli The depth of nuclear stain was less than that of the lymphocytes and neutrophils The cytoplasm was abundant, stained a pale blue with Wright's stain and Giemsa's stain The cell was quite large, 15 to 20 microns in diameter The cytoplasm contained from very few or no granules to abundant granules These were oxydase positive and were interpreted as azur granules

DR. FARLEY In 1913 Reschad and Schilling reported the first case where the term "monocytic leukemia" was used in the sense of a predominant hyperplasia of the monocytes with a supposed origin from the reticulo-endothelial system
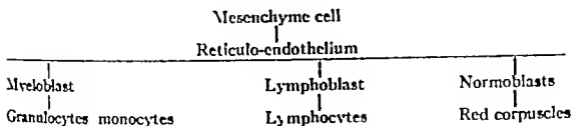
The Reticulo-endothelial System —It should be recalled that, briefly stated, we can include in the reticulo-endothelial system certain cells capable of phagocytizing colloidal particles present in the circulation in finely granular form, such as pyrrhol blue. The ability to store such particles distinguishes these cells from the other connective-tissue cells as well as from all

forms of myeloid and lymphatic cells The cells in question include many of the cells of the splenic pulp, of the medullary follicles and "cords" of the lymphatic nodes and of other lymphatic structures, of the splenic sinuses, of liver capillaries (stellate cells of Kupffer), of capillaries in the formative bone-marrow, and of the adrenal and pituitary The work of Aschoff (1924) should be consulted for more details of the subject

Grouping of Normal Leukocytes —Before going further, let us recall the appearance of the stained white cells of normal blood Judging from their morphology they appear to fall into three groups the granulocytes, the lymphocytes, and the monocytes The granulocytes include the eosinophils, the basophils and the neutrophils, possessing in common a multilobed nucleus and a cytoplasm containing many granules It seems proved that these cells arise from the myeloblasts of the bone-marrow The lymphocytes have a round or slightly lobulated nucleus and scanty cytoplasm There seems little question that these cells arise from the lymphoblasts of the lymphatic tissue But when we come to classify and state the origin of the third group of cells, the monocytes, we find much controversy It seems agreed, however, that the cells long counted separately as transitional and large mononuclear leukocytes, are identical They are now conveniently called monocytes The monocyte appears then as a cell larger than the lymphocyte and the granulocyte, with a round or horseshoe-shaped nucleus and abundant cytoplasm containing at times a few azur granules The chromatin of the nucleus is more loosely woven than that of the lymphocyte or granulocyte

Origin of the Monocyte —Ziegler (1908) held that monocytes were slightly differentiated myeloblasts Naegeli (1924) holds that monocytes are derived from myeloid cells Piney (1928) states that the origin of the monocyte is still uncertain. He considers the monocyte as derived from the myeloblast and as much a myeloid cell as any other granular leukocyte

His scheme of origin is

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                    Mesenchyme cell
                 Reticulo-endothelium
─────────────────────────────────────────────────
Myeloblast              Lymphoblast          Normoblasts
Granulocytes monocytes  Lymphocytes          Red corpuscles
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On the other hand, Schilling (1924) believes that monocytes are derived from the reticulo-endothelial system and have as separate and distinct an origin as the granulocytes and lymphocytes. Mallory refers to this cell as the endothelial leukocyte. He has considered them as desquamated endothelial cells from the lining of any blood or lymph channel.

Leukemia —The practical aspect of the origin of the monocyte becomes apparent in the classification of the different forms of leukemia. Are there three types of leukemia or only two forms? Is there such a condition as monocytic leukemia or is it merely a variant of myeloid leukemia? Naegeli and Piney and others believe that so-called monocytic leukemia is a form of myeloid leukemia. Reschad and Schilling and others would have us believe that it is distinct from both myeloid and lymphoid leukemia.

The oxydase stain is of no value in differentiating these cases since the monocytes are said to give positive reactions similar to the cells of the myeloid series.

The necropsy findings may be illustrated in a case reported by B. Swirtschewskaja (1928).

Spleen —The lymph nodules were practically absent. There was connective-tissue transformation and thickening of the stroma. The sinuses were dilated. The most striking changes were seen in the endothelial lining cells of the walls of the sinuses. These were swollen and exfoliated, the sinuses being filled with them. These cells were similar to the monocytic cells seen in the blood smears during life. There was no marked hyperplasia of these cells in the spleen.

Liver —There was dilatation of the capillaries, which were filled with cells like the endothelial cells of the splenic sinuses. Insignificant changes were present in the Kupffer cells. There

was no evidence of myeloid metaplasia in the spleen, liver or
other organs

Bone-marrow—There were small erythropoietic and gran-
ulopoietic foci   The marrow was diffusely filled with cells corre-
sponding to those of the spleen   The oxydase reaction was
positive in the granulopoietic foci and negative in the majority
of the cells of marrow   The same author states that according
to the degree of pathologic changes in the reticulo-endothelial
system, the published cases may be divided into two groups
In the first group there is a high degree of hyperplasia of the
reticulo-endothelial elements and an absence of hyperplasia of
the myeloid tissue   In the second group there is hyperplasia
of both the reticulo-endothelial and myeloid systems

In reviewing the literature we find that the course and prog-
nosis of monocytic leukemia differs little from that of myeloid
leukemia   Irradiation therapy offers the best hope for ameliora-
tion of symptoms in the chronic type   For the acute type little
can be done

This case is presented to draw attention to an interesting
form of leukemia   The diagnosis of monocytic leukemia is
open to question in the absence of necropsy   It is the opinion
of some that these cases should be classified as the monocytic
form of myeloid leukemia, while others would include them in a
separate group because of their conviction that monocytes have
as distinct an origin as the lymphocytes and granulocytes

The majority of the advocates of both points of view recog-
nize that the ultimate embryologic origin of all the cells of the
blood is reticulo-endothelium

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CHRONIC NON-TUBERCULOUS PULMONARY DISEASE

CONDITIONS which simulate pulmonary tuberculosis and cause confusion in diagnosis may show a likeness to the toxic type of tuberculosis Such varied conditions as hyperthyroidism, carcinoma, diabetes, and obscure focal infections may cause weakness, loss of strength, and weight, nutritional disturbances and skin and muscle changes which closely resemble the toxic effects of an early tuberculosis On the other hand, structural changes of an infective nature in the bronchial or pulmonary tissues may become chronic and be almost indistinguishable from tuberculous pulmonary involvement Among the conditions most frequently seen producing this picture are lung abscess, bronchiectasis, and localized empyema, particularly in an interlobar situation, which has ruptured and is draining through a bronchus

In each of these three conditions there is an infected area of suppuration where secretion or pus tends to accumulate and where infection is maintained Drainage is insufficient and surrounding lung tissue may be directly infected It is hard at times to differentiate these conditions, as their mechanism in producing symptoms is similar Bronchitis is apt to be persistent There may be periodic attacks of localized pulmonary infection There may be generalized or local bronchial spasm The x ray shows marked pulmonary involvement, but usually does not unquestionably reveal its nature The symptoms of chronic pulmonary involvement, with cavity formation and suppuration, are similar in all these conditions If the involvement is in the upper portion of the lung the differ-

entiation from tuberculosis is extremely difficult, if the apice are clear, there is less suspicion of its being tuberculosis

Pulmonary abscess not infrequently follows tonsillectomy It undoubtedly, in some cases, is the result of aspiration o tonsil tissue or infected tonsillar material, and the fact that i is relatively frequent following general anesthesia as compared with tonsillectomy done under local anesthetic makes it seem probable that aspiration is the important factor in its production On the other hand, it has been shown by Fetterolf that it may result from infected thrombus causing a pulmonary embolus, particularly where sutures are passed through the tonsil bed Pulmonary abscess occurs following pneumonia of various types With influenza an associated hemolytic streptococcus infection is apt to cause multiple abscesses These are usually small Pfeiffer bacillus infection may invade the bronchial walls so deeply as to cause perforation with resulting abscess Staphylococcus aureus infection may be associated with influenza and gives a characteristic picture of multiple lung abscesses, some of which may be large and persistent Friedlander's bacillus is exceedingly destructive to the lung tissue and characteristically causes abscess formation A foreign body lodged in a bronchus may result in bronchiectasis or lung abscess, and this condition is probably more common than is generally believed Dr Chevalier Jackson has discussed this question admirably

Bronchiectasis is frequent in fibroid pulmonary conditions apart from tuberculosis, as a result of influenza, of whooping cough, of gas inhalation—mustard, phosgene or chlorin It occurs in chronic bronchitis or pulmonary fibrosis resulting from other causes, as stonecutter's or miner's asthma, metal grinding inhalation of bronze powder in gilders, inhalation of molds or fungi as in threshers, and from many other causes The bronchial dilatation may be saccular or fusiform, single or multiple A particularly troublesome type shows dilatation of numerous terminal bronchi, generally distributed, particularly toward the bases of the lungs Where a large saccular dilatation occurs the whole picture may, as has been said resemble that of pulmonary abscess In the generalized and diffuse occurrence of terminal

lilatations the signs are, of course, widely distributed, and the picture is that of a persistent diffuse bronchitis

Interlobar empyema may occur after any type of pneumonia, or small localized collections may occur laterally or under the lung, firmly surrounded by adhesions forcing spontaneous drainage by rupture into a bronchus   The bronchus is reached by penetration through pulmonary tissue, and pulmonary infection takes place around this perforation

In each of these three conditions—abscess, bronchiectasis, and empyema—we are apt to have more or less extensive pulmonary infection and inflammation giving certain symptoms and signs. In each of them we are confronted with the necessity of establishing and maintaining drainage of the infected cavity before permanent healing of the pulmonary condition can take place. In the case of the empyema, external drainage can usually be accomplished satisfactorily   With pulmonary abscess this is much less likely to be so, and with bronchiectasis it can seldom be considered   In the two latter conditions drainage through the air passages must be facilitated and maintained   In any of these conditions where the disease has been present for some time the condition of the patient is apt to resemble tuberculosis in that cough, expectoration, febrile periods, progressive loss of strength and weight, loss of appetite and general weakness will be complained of   The x-ray may or may not give a clue leading to a diagnosis   Repeated examinations of the sputum for tubercle bacilli must be made   Where extensive tissue breakdown is evident and the sputum is frankly purulent the finding of tubercle bacilli may be reasonably expected in the course of relatively few examinations   A negative series of say 8 to 12 specimens argues strongly against the existence of tuberculosis as a cause of the trouble

If tuberculosis seems improbable bronchoscopic examination, which has been brought to a high point of delicacy and efficiency, may be of great service both in diagnosis and treatment. Bronchoscopic examination is serviceable and safe only if an expert bronchoscopist is available

Regarding x-ray examination, it must be said that a flat

plate can give only presumptive evidence It is almost im possible to note the outlines of a bronchiectatic cavity on such a plate Satisfactory stereoscopic views may show such cavities beautifully, but even with the stereoscope care and experience are usually necessary in making a diagnosis To the stereo-scopic views, lateral plates, which are usually serviceable only to one skilled in interpretation, and fluoroscopic observation may be added By the use of lipiodol injected by way of the trachea, a clear picture of the bronchial tract, dilatations, and cavities may sometimes be obtained

With the diagnosis of non-tuberculous cavity and accompany-ing bronchial and pulmonary disease, the question of treatment comes up If an encysted empyema lies at the root of the trou-ble the first treatment to be considered is surgical The simplest surgical procedure is the induction of a pneumothorax If the mediastinum is fixed by adhesions and a large portion of the pleura on the affected side is sufficiently free to allow collapse to take place, a cavity may be fairly well closed, secretion and infection diminished, and the general condition greatly im proved Such improvement should be soon apparent External drainage will probably be necessary for complete healing but the condition of the patient may be much more favorable for operation if a preliminary pneumothorax be induced If the cavity in question is due to dilated bronchus or to pulmonary abscess, it is unlikely that the opportunity for external drainage will present itself and we must effect as satisfactory a drainage as is possible by more limited measures, and the question of the advisability of a thoracoplastic operation may be consid ered Operation should be performed only by a surgeon who is experienced in chest work, who understands the physiology and mechanics of respiration and who appreciates the after-care necessary in subjects of pulmonary disease and chest surgery These patients cannot be sent to a general surgical ward to be operated upon and moved out to make room for other operative cases

If an efficient bronchoscopic clinic is available, endo-copic treatment, which may have to be maintained for a long period

of time may be satisfactory in establishing and continuing drainage, allowing shrinking of the cavity and healing by fibrosis Pneumothorax must be considered as an aid One advantage of pneumothorax as against phrenic exeresis is that if improvement does not promptly ensue, the pneumothorax can be discontinued while with phrenic nerve destruction the retraction of the diaphragm is permanent While collapse seems an excellent procedure in unilateral tuberculosis and while its results are often brilliant in collapsing a non tuberculous cavity, the inactivity of the lung tissue may be unfavorable in active pyogenic infection and may result in a retention of pus in the collapsed tissue In the event of induced pneumothorax this question must be borne in mind and conditions carefully observed

In the lung tissue surrounding an infected cavity there will be noted considerable density the extent of which varies from time to time Bronchitis, localized or diffused, will be apparent, and periods of bronchial spasm, which frequently are localized to the region of the affection, will be noted Hard coughing tends to empty the cavity and the bronchial tract In the event of spasm or obstruction of larger bronchi coughing may result in a forcing backward of infected material, causing bronchiolitis and pneumonitis in the area thus invaded This mechanism is probably responsible for the localized areas of bronchopneumonia which occur repeatedly in these conditions Satisfactory drainage requires that the removed material not only leave the cavity and the surrounding bronchi, but also be completely removed from the trachea without being forced back into other bronchial branches The handling of this condition which might be called a local asthma (which has been noted by Jackson in cases of foreign body) is highly important Bronchial relaxation may sometimes be satisfactorily maintained by very small doses of belladonna preparations I have had little experience in relying on ephedrin for long continued relaxation, although it seems possible that exceedingly small doses of this drug might be satisfactory

The use of autogenous vaccines seems to me the best method in the majority of patients Vaccine may be very effective in

treatment   Its effect may be independent of any increase of
the immunity of the patient to infecting organisms   Its effect
in reducing bronchial spasm is often very marked, and by this
means drainage is enhanced and back-pressure under coughing
avoided   Vaccine must be used for a long period of time   I
have used vaccines prepared by Dr John L Laird, Chief of the
Laboratories of the Pennsylvania State Board of Health   The
first patient whom I treated by this method was seen in 1910
She showed a large abscess of the right upper lobe with extensive
infection of the lung   She had been seen by several consultants
and was told she was suffering from pulmonary tuberculosis and
had been advised that residence in the southwest was her only
possible chance of recovery   She did extremely well under
treatment, and while she had three relapses during ten or twelve
years, they were brief and yielded well to treatment on each
occasion   I last saw her fifteen years after the beginning of the
treatment, at which time she was in good health   Dr Laird
makes a mass growth of the sputum on three different media,
with no attempt at separating various organisms   He grows
the cultures as rapidly as possible and sterilizes with as little
heat as will give effective sterilization   His emulsion yields ap-
proximately ten billion organisms per c c   It is watched care
fully for spores before being used   Injections are started at
about 1/100 c c and increased gradually to 1 c c at about a
five-day interval   Dr F W Burge, who has treated a great
many patients in the city chest clinics and the Medical Dis-
pensary of the University Hospital by this method, feels that
multiple injections of vaccine are more effectual than single
injections   He divides the dose to be given into from 2 to 10
portions and injects at different sites   Drs Stengel and Fox
some years ago reported a series of 13 cases of bronchiectasis
treated in the University Hospital wards by vaccine with satis-
factory results   Dr Fox washed the sputum and endeavored to
obtain the predominant organism, preparing his vaccine there-
from   Dr Moffet, of Harrisburg, has worked for a number of
years with the Chevalier Jackson Bronchoscopic Clinic at the
Jefferson Hospital's Chest Department, and advocates the use

of autogenous vaccines in pulmonary infection and particularly in bronchitic asthma He has fully described his methods of preparing the vaccines I have found Dr Laird's method extremely satisfactory

Creosote is of great service in bronchial and pulmonary infections if it can be introduced into the system in sufficient quantity to show a good concentration in the bronchial secretion The preparation called "calcreose" offers a convenient and serviceable method of administering creosote in fairly large amounts. It is usually well tolerated by the stomach A 4-grain tablet of calcreose is said to carry 2 minims of creosote and from 6 to 8 such tablets can easily be taken daily without upsetting the stomach This seems to have a soothing effect on the irritated bronchus and to allay bronchial spasm to some extent I believe that it shows a definite influence in checking bacterial growth in the bronchial contents

Drainage may further be aided by postural changes If the body be turned the dependent portion of the cavities will be raised and secretion directed therefrom toward an open bronchus whence it can be expelled A routine measure for patients with cavity is as follows For "postural treatments" one end of a board or shutter, about 5 or 6 feet long, is placed on a table or desk in such a way as to raise the end about 3 feet from the floor The patient lies on the back with the head at the lower end and breathes deeply, extending the arms to aid full respiration This process is repeated, lying successively on the right and left side and on the face This procedure is gone through twice a day This will usually provoke coughing and increased expectoration at first, but on continuing these exercises the cough and secretion diminish It is surprising how much can be accomplished with the faithful use of postural exercises, vaccine, creosote, and possibly other measures for the reduction of bronchial spasm These methods of treatment may be combined with bronchoscopic treatments if these are available A long-continued course and not infrequent relapses may be expected, but on the whole, a fairly satisfactory result can usually be obtained In general cavities situated in the upper

lobe respond well to treatment   This is noted in the cases re ported by bronchoscopists as well as in those cases where treatment was wholly medical   Lower lobe abscesses are much less amenable to satisfactory treatment by any method

A type of bronchial or pulmonary irritation which may be difficult to understand is found in connection with chronic upper respiratory infection, particularly obstinate infectious ethmoiditis Where ethmoid disease has been present for some time a bronchitis is apt to be found in association with it   x-Ray studies of the chest at this stage will show a heavy peribronchial exudate, particularly marked in the hilus region and radiating outward along the bronchial divisions toward the base and even toward the apex   This exudate is dense enough to suggest fibrosis, but may disappear so completely as to make it certain that the condition is exudative rather than proliferative in nature   Post nasal infection with disease of the ethmoid or other sinuses has been extremely prevalent during the past few years   It would seem that certain strains of organisms became very widely implanted in connection with the flu epidemic of 1918, at which time all sufferers from influenza appeared to acquire sinus disease, and that this infection has been transmitted very widely since that time   If a patient shows a troublesome diffuse bronchitis, possibly with patches of pulmonary infection, constitutional symptoms indicating absorption, a postnasal catarrh, streaks of inflamed red tissue behind the posterior tonsillar pillars, and flecks of red lymphoid tissue on the posterior pharynx wall, infection of the postnasal sinuses may be suspected   Mucopus will be seen in the postpharynx and characteristic symptoms of ethmoid disease will be complained of upon inquiry   x-Ray of the sinuses will probably show clouded ethmoids   The chest picture is quite characteristic and a few years ago these chests were quite regularly reported by the roentgenologist as showing tuberculous infiltration   A more conservative view is now generally taken   In making a diagnosis in these conditions we again must depend a great deal upon the laboratory as the constitutional symptoms of chronic infection are very similar whether that infection be streptococcic infection

of the sinuses or tuberculous infection of the pulmonary tissue Repeated examination of the sputum, if negative, is of great value in classifying these cases Symptomatic improvement under regular treatment of the postnasal area is also valuable in forming conclusions regarding the nature of the case

It was noted, as far as I know, first by Dr Eves that children with ethmoid disease were apt to be temporarily better after having an x ray picture of the sinuses taken and he suggested therapeutic x-ray exposure of this region and stated that he got good results from this procedure Dr Bromer, at the Orthopedic Hospital, has treated a number of patients with chronic ethmoid disease by mild radiation of the ethmoid region, giving five or six treatments at an interval of several days He has had no bad results and there has been marked improvement in all but one of between 15 and 20 cases The bronchitis and peribronchial exudate diminish rapidly as the ethmoid infection clears up

The nature of the bronchial and pulmonary involvement in these cases is not altogether clear Certain facts regarding pulmonary exudates have long been recognized Following pneumonia more or less extensive exudate may remain unresolved for long periods of time This occurs in the presence of chronic infection, as tuberculosis, and is particularly striking in the presence of syphilis It is my impression that exudates persist also in association with persistent thymus gland in the so-called thymolymphatic individuals It may be that chronic infection of the ethmoids simulates tuberculosis in the tendency to persistence of exudate as it does symptomatically in many other respects. Certain types of influenzal pneumonia are accompanied by dense round-cell infiltration surrounding the bronchial trunks and branches of all size This has been well shown at autopsy We have no autopsy records relating to the cases in question where the condition clears up satisfactorily, but the general resemblance in the x-ray findings between these cases and the postinfluenzal chests is so striking that it seems probable that the structure of the exudate is very similar In the post influenzal cases much of the exudate disappears completely with

surprising suddenness   Where suppuration has taken place per
manent fibrosis may result and frequently this fibrosis is very
extensive, but in the great majority of patients observed the
disappearance of the exudate was fairly complete   In lues per
sistent exudates may be massive and have been observed to last
for months and even for years with prompt and complete clear
ing under specific treatment

In tuberculosis it is harder to judge such conditions as 'the
picture is complicated by the tuberculous infiltration of the
lung and extensive fibrosis   In the chronic ethmoid cases the
result in a single case may be hard to judge, but in considering
a large number of patients the effect of treatment seems un
doubted and remarkably satisfactory

In the case of a patient showing persistent peribronchial or
pulmonary exudate, we should look in the first place for evi
dence of lues, tuberculosis, or other chronic systemic infection
Further search must be made for chronic focal infection, par
ticularly of the postnasal sinuses   The symptoms and signs of
this trouble are usually fairly conclusive   If tuberculosis and
syphilis can be reasonably ruled out and postnasal infection is
found, this latter condition must be vigorously attacked   Oper
ative interference with the ethmoid cells, while sometimes neces
sary, is always hazardous and usually unsatisfactory   I believe
it should be advised or permitted only as a matter of necessity
or under the gravest indications

Badly infected tonsils may be responsible for the persistence
of postnasal infection   Tonsillectomy may permit a clearing up
of the infection   Regular treatments of the nose by shrinking
may permit a satisfactory clearing of the condition   Removing
of turbinates or septal spurs to allow ventilation, may be neces
sary   The patient, may on moving to a dry climate and high
altitude, secure fairly prompt and permanent relief from the
sinus infection   If regular intranasal treatments at least three
times a week are not practicable, the use of ephedrin in 3 per
cent aqueous solution, with a medicine-dropper or atomizer,
three or four times daily and as occasion requires, may keep
the nose free, giving ventilation, and by shrinking the post

nasal tissues allow adequate and continuous drainage of the ethmoid cells Small doses of belladonna preparations or atropin may aid greatly in keeping the nose clear If these procedures are not successful in clearing up the infected area, x ray of the sinuses may accomplish this end Medical treatment of the chest condition is simply the treatment of the co-existing bronchitis Iodid in small doses may be of particular service Creosote is useful Where peribronchial or pulmonary infiltration is persistent, radiation by the x ray may produce an immediate clearing up of this exudate.

CLINIC OF DRS GARFIELD G DUNCAN AND
DAVID S POLK

FROM THE CLINICS OF DR THOMAS MCCRAE, PENNSYLVANIA AND
JEFFERSON HOSPITALS

THE HYPOGLYCEMIA HAZARD IN THE TREATMENT OF DIABETES MELLITUS

HYPOGLYCEMIA presents cause for real concern in certain diabetics Children and undernourished adults are most susceptible to the extraneous influences which tend to lower the blood-sugar The latter group has provided most of the fatalities reported as being due to hypoglycemia Such accidents are preventable, they do not justify the too prevalent though decreasing antipathy toward the use of insulin when it is indicated

Abnormally low blood sugar figures have been found in non diabetics following strenuous exercises diarrhea, vomiting and fasting It is not surprising then that these factors influence the level of the blood sugar in the insulin-treated patients also

The prompt effectiveness of insulin has increased the necessity for accurate treatment if an uneventful course between hyperglycemia and hypoglycemia is to be enjoyed The practice of permitting hyperglycemia and even glycosuria in an effort to prevent a low blood sugar is—it is obvious—merely making a severe diabetes appear mild. The susceptibility to infection remains, the disease as well as arteriosclerosis progresses and freedom from symptoms is denied.

The level of the blood sugar at which symptoms of hypoglycemia appear varies considerably John[1] reports having found a blood-sugar within or above normal in 10 patients suffering symptoms typical of a hypoglycemia On the other hand, Joslin's[2] patient with a blood-sugar of 030 per cent. was free from subjective symptoms The familiar signs may or-

dinarily be anticipated when the blood-sugar falls below 060 per cent   During a gastro-intestinal upset Smith's[6] patient had no demonstrable sugar in the blood

Case I (No 1887) —White, male, age forty-five, was admitted to Dr McCrae's service at the Pennsylvania Hospital, October 27, 1928, in a comatose condition   Record of previous admissions, November 30, 1927 and February 10, 1928, revealed on respective discharges blood-sugar 0 140 per cent , blood-pressure, 126 systolic, 80 diastolic, weight, 111 pounds, 10 units of insulin daily, and blood-sugar 0 171 per cent , weight, 114 pounds, and 45 units of insulin daily   He enjoyed good health in the interval between the second and present admissions Prior to the morning meal October 27, 1928 (date of admission) a friend administered the insulin, and it was evident later that a mistake was made in measuring the dose   During the forenoon he was actively engaged in his usual occupation   No insulin or food was taken at noon   When he met his daughter at 1 10 P M , by appointment, she observed that he was pale, weak, perspiring, trembling, claw-handed, and cross-eyed

At 2 15 P M , when he was admitted to the hospital, he was quite unconscious, the skin was pale, moist and cold, there were irregular spastic contractions of the muscles of face, arms, and legs, the eyes were closed with orbits turned toward the midline and there was Cheyne-Stokes respiration with periods of apnea lasting from ten to twelve seconds   The heart sounds were irregular in force and rhythm, the blood-pressure was 160/100, the temperature (rectal) was 97° F and the blood-sugar was 0 023 per cent (Folin Wu)

At 2 25 P M 10 c c of a 50 per cent solution of glucose was given intravenously and an almost immediate response was noted, the respirations became deeper and more regular, but he continued to be restless and consciousness was not regained

At 2 45 P M 300 c c of a 10 per cent solution of glucose was given intravenously   The pulse volume and respirations improved, the muscular efforts were more marked and there was a change from stupor to active delirium

At 4 00 P M the pulse was 126 and irregular in rhythm, and the respirations were 40 Orange juice (100 c c) was given by mouth The patient became quieter

At 5 00 P M he was in profound shock, the muscular efforts having ceased, the respirations were slower, and the pulse imperceptible. The blood sugar was 0 010 per cent Later the respirations practically ceased and the heart sounds could not be heard Artificial respiration was begun and epinephrine (15 minims of a 1 1000 solution) and caffeine sodium benzoate gr 6 were given intramuscularly with 35 gm of glucose intravenously and 35 gm. subcutaneously

At 5 45 P M he was restless and struggled vigorously This was followed by quiet and sleep

At 8 00 P M 50 gm of glucose were given by nasal catheter, these were well received and retained

At 10 00 P M 200 c c. of orange juice were given by mouth with some objection

At 11 30 P M consciousness returned, but he resisted efforts to feed him, 100 c.c. of orange juice were given and repeated at 12 15 A M

At 2 30 A M the patient sat up and took nourishment. He was mentally clear and his general condition was good, but he could not remember anything that had taken place since 1 15 P M the previous day

He was discharged on November 3, 1928, taking 20 units of insulin daily as compared with 40 units prior to admission The fasting blood sugar was 0 114 per cent , the blood pressure 112/76, and weight 113 pounds

Case II (A3214) —A mechanic, fifty years of age, weighing 138 pounds, was unconscious when admitted to Dr McCrae's service at Jefferson Hospital May 9, 1929 The respirations were full, the pulse 80, of good volume, the temperature 96° F (rectal), the skin moist, the pupils dilated, and the reflexes normal The blood pressure was 150/90 and the blood sugar 0 021 per cent

The usual dose of insulin (25 units) had been taken before

breakfast and 15 units at 5 P M   When returning from work at
5 20 P M he "felt dizzy," and this symptom increased until he
was forced to sit down on some steps   This was the last recol-
lection he had   He was found unconscious and brought to the
hospital   At 7 45 P M 50 gm of glucose in a 25 per cent solu-
tion were given intravenously, and consciousness soon returned
He had 1 per cent of sugar in the urine at 10 00 P M in spite
of a blood-sugar of 0 031 per cent   His recovery was uneventful
The blood-pressure on successive days prior to discharge was
110/68 and 130/72

Comment —In each patient the blood-pressure, though
known to be normal, prior to and after the attack, was found
distinctly increased during a certain period of the hypoglycemia,
thus agreeing with Wilder's[7] observation   A fall in blood-pressure
occurred during what appeared to be a terminal stage   Are the
cerebral hemorrhages occasionally found in patients supposed
to have died from acidosis due to the increase in blood-pressure
when too small amounts of or no glucose is used as a safeguard to
prevent hypoglycemia?   The patient dying of diabetic coma
dies from acidosis, not hyperglycemia   Is it not safer to maintain
a moderate hyperglycemia until the acidosis is corrected and
consciousness restored?

The tendency of the blood-sugar to return to subnormal
levels after improvement has occurred indicates the necessity
of frequent administrations of glucose until it is obvious that
such precautions are no longer necessary   Case II illustrates
the return of hypoglycemia even after glycosuria had been pro-
duced   The same total amount of glucose, but given in divided
doses, thus preventing loss of sugar in the urine, would probably
have served to increase the blood-sugar sufficient to obviate the
likelihood of further hypoglycemia

Common Factors Affecting the Level of the Blood-sugar and
the Insulin Requirement —1 *Overcoming Hyperglycemia* —Con-
trol of the diabetes through the agency of an accurate diet and
insulin is followed by a rapid or gradual decrease in the insulin
necessary   Whether this is actual gain in tolerance or a lowered
insulin requirement following the metabolism of excess sugar in

the tissues and blood does not matter for practical purposes Decrease of all doses may be necessary Ordinarily a reduction of 2 to 8 units suffices when a single dose is being lowered, the reduction being from the dose corresponding in time to the one preceding the hypoglycemia or the finding of a blood sugar at the lower border of normal

2 *Diet* —(*a*) An undernutrition diet facilitates the reduction of a blood-sugar and is an important factor in producing hypoglycemic attacks if appropriate reductions in insulin are not made At this point, it may be stated that with diets containing a moderately high carbohydrate content, the insulin requirement tends to decrease from year to year [8] On high fat diets with low carbohydrate contents the tendency is for the insulin dosage to remain stationary or increase after the initial drop which follows the control of the disorder

(*b*) Irregular distribution of the diet from day to day yet with the same total number of grams of protein, fat, and carbohydrate, is frequently responsible for fluctuations in the blood-sugar sufficient to cause a hypoglycemic reaction one day and a hyperglycemia at the same hour on the succeeding day, with insulin constant An accurate dosage and distribution of insulin may be obtained only if each meal conforms closely in value to the corresponding meal the day previous Whether or not the diet is equally divided into three meals does not matter Parallelism of the corresponding meals, particularly in the carbohydrate content, is the important feature

(*c*) Omission of a meal, diarrhea, or vomiting, after the insulin has been taken is an occurrence which occasionally has to be handled Loss of appetite rarely prevents the patient taking ample carbohydrate in liquid form The combination of sodium bicarbonate and sodium chlorid, of each $\frac{1}{2}$ dram, given in water by mouth, has proved a valuable aid in overcoming vomiting, though usually expelled, it enables the retention of carbohydrate in liquid form

3 *Infection and Acidosis* —Rapid increase in tolerance when relief from acidosis was secured and a gangrenous foot amputated is illustrated in Case 3204 of the Physiatric Institute Series [10]

From 146 units given in six doses the daily requirement fell to 16 units given in two doses without any sign or symptom of hypoglycemia, yet with satisfactory blood-sugar figures   Case 1574 of the same, series[9] with pneumonia (lobar) and acidosis required 254 units in six doses during the first twenty-four hours, yet five weeks later, 70 units in three doses proved ample to maintain control of the diabetes   On two occasions mild symptoms of overdosage were recorded   Fear, which might have prevented the use of insulin, would doubtless have proved fatal in these two instances   They illustrate further the necessity of reduction of insulin and the ease with which hypoglycemic reactions of any import may be avoided even when large doses are administered

4 *Insulin*   (*a*) Changes in the dosage   When the diet-insulin balance (proper amount and distribution of insulin to keep the blood-sugar figures normal with a diet sufficient to maintain the body weight at the desired level) is nearly established, changes of 1 or 2 units suffice   Allen[11] reports profound symptoms following changes of $\frac{1}{2}$ unit, while one of Joslin's[4] patients became comatose from hypoglycemia when 1 unit was added to the usual dose   The prevalent habit of increasing and decreasing insulin in multiples of five should be censured   We see too frequently undernourished patients with severe diabetes deprived of an available safety zone by the shuttling back and forth of the blood-sugar from one extreme to the other by such changes

(*b*) Distribution   Rarely do two or three equal doses of insulin suffice to maintain normal blood-sugar figures throughout the twenty-four hours   The total may be correct, yet hypoglycemia occurs in the afternoon or evening and a hyperglycemia exists in the morning   A simple plan enabling the proper division of the total unitage is to examine qualitatively for sugar a specimen of urine voided before each meal   For example, the 7 A M and 11 A M specimens are free from sugar, but the 4 P M voiding gives a moderate reaction for sugar   It is obvious that the noon dose of insulin on the succeeding day should be increased   As the doses are increased in this fashion in the severe

diabetic, low blood sugar levels may still be encountered during the day time with hyperglycemia in the morning. Except in the very severe, in which four doses are necessary, this difficulty may be overcome by Allen's[1a] plan of lengthening the day periods between insulin administrations and shortening the night period by giving the morning dose one hour before breakfast and the evening dose one hour after supper or even at bed time. Occasional blood analyses are necessary to guide further increases after the urine becomes free from sugar.

5. *Exercise.*—The blood sugar lowering effect of exercise is manifested in the diabetic as well as in the non-diabetic. A patient may be free from reaction and have normal blood sugar figures for long periods and yet have a severe hypoglycemia after unusual exercise. One private patient, Mr. E. S., ordinarily requiring 20 units per day, has learned to reduce the dose preceding a game of golf by 4 units. One of Joslin's[5] patients, taking 25 units, has found that a reduction of 5 units is necessary to prevent hypoglycemia following golf.

Immediate Control of the Low Blood-sugar.—There should be no difficulty in recognizing a hypoglycemic reaction. The moist skin, normal intra-ocular tension, absence of dehydration, air hunger, and plasma acetone, normal or increased blood-pressure, unless in terminal state, the usual freedom from glycosuria and the recently reported extensor response[13] on plantar stimulation, readily differentiate the condition from acidosis.

Intravenous glucose administration may be essential. Moderate amounts should be given by this route or subcutaneously at frequent intervals, fifteen to twenty minutes, until retention by mouth is allowed. The possibility of retention of carbohydrate in the stomach with little or no absorption is to be kept in mind. The giving of 10 gm. of carbohydrate by mouth may be continued every half hour with advantage in the severe cases until glycosuria occurs. Such a patient as Case I requires close watching for the ensuing twelve hours.

The practice of carrying glucose or syrup to be taken if symptoms of hypoglycemia appear is a good one. The diabetic identification card suggested by John[2] has definite value.

The likelihood of hypoglycemia occurring is reduced to a minimum and the dangers are practically nil if the simple rules governing the changing of dosage and distribution of insulin outlined are observed, parallelism of the carbohydrate content of the corresponding meals maintained, and the daily exercise kept nearly uniform in time and amount

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FAILURE OF SALT RESTRICTION IN THE TREATMENT OF HYPERTENSION

AMONG the multiplicity of treatments recommended for patients with high blood pressure, limitation of the amount of sodium chlorid ingested occupies a prominent place Ambard, Laufer, and other French writers advocated salt poor diets for hypertension as early as 1904 and salt restriction is still a popular method of treatment for hypertension in France Many German workers however, including Loeb Brodski and Lowenstein, have published unfavorable reports with the use of such diets The attention of American physicians was first aroused by Allen,[1] who, on the basis of his own studies, in 1920 published records of 20 patients with hypertension who were symptomatically improved, and whose blood pressures were reduced by salt poor diets Allen also reported that administration of sodium chlorid was followed by a rise in blood pressure in this group

During the past eight years a number of papers dealing with the results of salt poor diets in the treatment of hypertension have appeared in the American literature, but without any unanimity of opinion concerning its value Musser, Komkow and Smith, Houghton, Duncan and Rudy and Blaisdell believe that sodium chlorid retention is the cause or is at least intimately concerned with hypertension, and that its limitation is the best method of treatment McLester, O'Hare and Walker, Christian and Strauss are skeptical of the etiologic relationship of sodium chlorid to hypertension, and have been unable to confirm Allen's results

As to the theory back of the restriction of sodium chlorid, Allen[2] says that his work was first suggested by "the cases of hyposthenuria and polyuria, the plan being to stop the excessive day and night strain upon the kidney and circulation by omitting salt, thus obviating thirst and polyuria, and to observe the benefit to blood-pressure and other symptoms   The benefits obtained in such cases were then duplicated in cases without polyuria "   Allen insists that to obtain benefit the restriction in salt intake in many cases must be extreme, and treatment is only considered adequate when the total chlorid in the urine, calculated as NaCl, averages 0 5 gm a day or lower   In some instances it was necessary to continue this rigid restriction for months before any lowering of blood-pressure was observed   In 1920 Allen and Sherrill reported a series of 180 cases of hypertension of various types treated by sodium chlorid restriction, with benefit in 70 per cent

During the past three years there have been 41 patients discharged from the medical wards of the Hospital of the University of Pennsylvania with a diagnosis of either essential hypertension, or arteriosclerosis with hypertension, whose systolic blood-pressure on admission was 170 mm or over   Twenty of these had been given the ordinary hospital diets, while 21 had been given a salt-poor diet   This diet contains about 2000 calories and about 1 5 gm of NaCl   The ages, sex distribution, hospital stay, and initial blood-pressure range of the two groups were very similar (Table I)   Of the 21 patients given a salt-

TABLE I

COMPARISON OF EFFECTS OF ROUTINE "SALT-POOR" AND FULL DIETS ON SYSTOLIC BLOOD-PRESSURE

Diet	No of patients	Ages	Days in hospital	Systolic blood-pressure on admission.	Number showing 10 mm. or more change in blood pressure.		No change.
					Fall	Rise	
Salt poor	21	27–72	5–40 average 19	170/253	9	2	10
House	20	30–60	4–30 average 18	176/240	16	1	3

poor diet, 9 showed a fall in systolic pressure of 10 mm or more during their stay in the hospital, while of the 20 given the full diet, 16 showed a fall in pressure This may be taken as evidence that a routine salt poor diet, as carried out on the wards, is of no benefit, and as Dr Joseph Miller once remarked, imposes a hardship without results, and is a constant reminder to these patients that they are sick Physicians who are convinced of the benefit of salt restriction might feel that if the diets had been continued for a longer period the patients who denied themselves salt would ultimately have been better off than the others But variation in blood pressure level in essential hypertension is affected markedly by many factors especially a change in mode of living, worry, and nervous strain. In other patients improvement in cardiac reserve with rest or removal of some complicating factor is followed by a fall in blood pressure Even in normal individuals undernutrition may lead to a fall in blood pressure [3] Because of the great number of conditions under which marked changes in blood pressure level occur, it is difficult to attribute changes during a long period to a reduced salt ingestion with any degree of confidence unless the patient has been under the closest observation throughout

It is admitted that the diets given these patients were not as low in salt as those recommended by Allen. Therefore I wish to present briefly histories of 3 patients who were subjected to a more rigid regimen All were kept at rest in the hospital for some time before being given the salt poor diet so that the fall in blood pressure which is frequently seen after a few days' hospitalization, would not be erroneously attributed to the diet.

Case I —J G , a white male, thirty six years of age, was admitted to the Medical Division of the Hospital of the University of Pennsylvania on March 26, 1928 complaining of severe headaches and "bilous attacks " Physical examination showed moderate arteriosclerosis, heart enlarged to the left, and a blood pressure of 285 systolic, 170 diastolic. His father, sixty-nine years of age, has a blood pressure of 205/120, his mother,

who was five years younger, a blood-pressure of 200/100   One sister, twenty-four years of age, also had hypertension (145/85), while in two other siblings blood-pressures were within normal limits   His urine contained albumin and hyaline casts   Blood-urea nitrogen was 18 mg per 100 c c , phenolphthalein output 25 per cent the first hour and 15 per cent the second   A two-hour concentration test showed a variation in specific gravity from 1 008 to 1 017, day output 320 c c , night 950 c c   After drinking a liter of water 716 c c were excreted in three hours   His condition was believed to be arteriosclerosis and hypertension, with arteriolar-nephrosclerosis

For seventeen days after admission he spent most of the time in bed, but was allowed the full hospital diet   His blood-pressure fell slightly, the lowest record being 235/120, usually it was about 250/165   He felt much better and had very little headache   During the following three and one-half weeks, until he left the hospital, he was given a salt-poor diet, calculated to contain about 0 55 gm salt   The chlorid excretion in his urine, calculated as NaCl, fell from 5 36 gm the first day of salt restriction to 0 36 gm on the day of discharge   For the last eleven days it was less than 1 5 gm on all but one day   His blood-pressure showed no sustained fall, although a single reading of 215/155 was obtained   The morning before discharge while at rest in bed, his blood-pressure was 255/170

Case II —J H , white, aged forty-six, was admitted to the service of Dr Arthur Newlin in the Pennsylvania Hospital, September 10, 1927, complaining of swelling of his ankles   He gave a history of repeated attacks of sore throat from 1917 to 1919   He had begun to notice dyspnea on exertion and swelling of his ankles in June, 1927   Physical examination showed marked retinal sclerosis, an enlarged heart, slight edema of the ankles, tortuous, thickened arteries, and a blood-pressure of 190/125   His urine contained a trace of albumin   His blood-urea nitrogen was 50 mg per 100 c c , phenolphthalein output less than 10 per cent in two hours   A concentration test showed a fixation of urinary specific gravity between 1 009 and 1 012, while after

drinking 1500 c.c of water he voided only 450 c.c in six hours He was believed to have chronic nephritis, hypertension, and beginning cardiac decompensation With five days' rest in bed his edema disappeared, he felt better, and his blood pressure fell to 170/100

He was then given a salt poor diet for twelve days, on which his chlorid excretion (as NaCl) fell from 10 9 gm the first day to 0 34 gm, with an average of 0.5 gm per day for the last four days During this period he was free from symptoms and his blood pressure had fallen to 138/80 If the salt restriction was responsible for the fall in blood pressure, administration of salt might be expected to be followed by a rise in pressure

Accordingly, for the next ten days 10 gm of NaCl were added to the same diet he had been taking, and in order to persuade him to remain in the hospital, he was allowed out of bed The addition of salt was not followed by any return of symptoms nor by any significant change in blood pressure, the highest reading obtained being 150/80, and the lowest 130/80

Case III—D A, a white male of sixty years, was admitted to the service of Dr Arthur Newlin in the Pennsylvania Hospital, April 30, 1928, complaining of failing vision and swelling of the legs, which had grown progressively worse during the four months before admission Physical examination showed proliferative retinitis, a moderate amount of fluid in both pleural cavities, an enlarged heart, enlargement of the liver, and edema of the lower extremities as high as the knees His peripheral arteries were tortuous and thickened His blood pressure was 285/120 His urine varied from 1 005 to 1 023 in specific gravity, and contained a cloud of albumin The blood-urea nitrogen was 26 mg per 100 c c at one estimation, 32 mg at another Phenol phthalein output after intramuscular injection was 10 per cent the first hour and 20 per cent the second The diagnosis was arteriosclerotic kidneys, general arteriosclerosis with hypertension and beginning cardiac failure

He was placed on a low protein diet with moderate sodium chlorid restriction for four weeks His edema rapidly disap

peared, and he felt much better   His blood-pressure fell to
180/80

For the next six weeks sodium chlorid was more definitely
restricted   His total urinary chlorid, expressed as NaCl, aver-
aged 0 76 gm per day for the last three weeks and frequently
was below 0 4 gm   His blood-pressure during this period ranged
from 160/90 to 235/115, most of the readings being around
190/95

Then for a period of two weeks 8 gm of NaCl daily were
added to the same diet with no effect on his blood-pressure, the
highest record being 230/110

In these 3 patients, in whom an attempt was made to restrict
rigidly the sodium chlorid intake, no reduction of blood-pressure
attributable to the salt restriction was evident during the period
of observation   It may be objected that the periods of study
were not sufficiently long   If salt restriction itself has any effect
on blood-pressure this should be demonstrated when the salt
stores in the body have been depleted   Unexplained variations
in blood-pressure, especially a reduction after months or years of
hypertension, are commonly encountered in middle-aged pa-
tients under observation for long periods

So far as my personal experience goes, I have not been able
to recognize any reduction of high blood-pressures which I
could attribute with confidence to salt restriction, nor does a
critical review of the literature persuade me of its value

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CHRONIC DUODENAL ILEUS

THE patients whose records I wish to present today represent two types of duodenal obstruction Their clinical pictures will be discussed in connection with the findings in a series of 40 such cases that have been studied in this hospital during recent years Various names are applied to these cases, such as chronic duodenal ileus, stenosis of the duodenum, arteriomesenteric ileus, and megaduodenum Each of these is in some measure descriptive of the underlying pathology This, in a word, consists of partial and chronic occlusion of the duodenum with resultant stasis, and possibly secondary dilatation and hypertrophy

Occlusion is brought about usually by one of two factors First, by pressure of peritoneal folds or bands of either inflammatory or congenital origin, and, second, by compression by the mesenteric root where it crosses the duodenum in its third part Concerning congenital folds much has been written, and opinion seems to be unanimous that embryologic defects or lack of development may operate in later life to produce the syndrome described Kirk's band, Harris' membrane, the ligament of Treitz, and other less well-defined membranes are seen not infrequently at operating and postmortem tables Folds of inflammatory nature, whether from disease of gall bladder, duodenal ulcer, or any other cause, may operate in exactly the same fashion On the other hand, concerning occlusion due to pressure by mesenteric vessels, less is understood But there is a growing conviction that, while a certain degree of stasis from this cause may be physiologic, as Glénard[1] has pointed out, exaggerated

forms of it are fraught with discomfort and danger to the in-
dividual Exaggeration of this is most noticeable in individuals
of ptotic habitus, in whom coils of enteron lie low in the pelvis,
thus dragging on the mesenteric root with resultant constriction
of the duodenum, in cases of gastroptosis and gastrectasis
wherein the heavy stomach lies low and causes consequent
kinking and stasis at the duodenal outlet, or in patients with
marked lordosis or other deformity of the spine which causes
posterior duodenal compression In a word, any cause which
lessens the mesenterico-vertebral angle may produce chronic
duodenal ileus

Clinical interest in these cases lies in the facts that the
group is still rather ill-defined and that the symptoms are
usually misinterpreted In general, the symptomatology is sug-
gestive of one of two other groups of cases First, cases are en-
countered with symptoms arising chiefly from stasis and from
the absorption of toxic products in the duodenum These pa-
tients' complaints are often vague, and as a result they are apt
to be classified as functional cases, or as neuroses Second,
cases are observed whose symptoms simulate in many respects
such definite organic disease as peptic ulcer or cholecystitis

According to Kellogg and Kellogg[2] the earliest recorded case
of chronic duodenal ileus is that of Boerneus in 1752 It was
not until 1900 however that there began to be any wide-spread
recognition of the condition as an entity and that reports
began to appear commonly in the literature Since that time
these have been numerous in both English and foreign lan-
guages The condition however, seems to be not commonly
recognized in practice and it was with the idea of helping to
define more clearly this group that 40 cases from the medical
and surgical services of the University Hospital were studied
The cases presented here have been chosen from the group men-
tioned because they are felt to be illustrative of certain phases
of the syndrome, particularly of the two main types of symptoms,
of the two main pathologic conditions, and of the two chief
means of surgical relief

Case I —L S , a woman of thirty three years, was admitted to the medical ward February 2, 1928, complaining of "gas on stomach" and weakness She had suffered indigestion since childhood but it had never been very troublesome until ten years prior to admission At that time she had "a general breakdown " and in addition to malaise and palpitation she developed aching and discomfort in the right side of her abdomen Subsequently she complained of eructations and dis tention with some pain in the rectum on defecation, constipation, and occasional blood in the stool Appetite was poor, and she had lost thirty six pounds in weight Nausea was occasionally present, but no vomiting On admission she complained also of nervousness, sleeplessness, and palpitation, as well as of head aches and mental depression In addition, there were some vague joint symptoms

Her past medical history was unimportant The important items in her family history were that her mother died of tuber culosis and that her grandfather and father both suffered from psychoses Social history stated that the patient, a clerk, had been unable to work for seven years because of illness and that she cried and worried a good deal about financial conditions, although matters at home were comfortable

Physical examination revealed a nervous, apprehensive woman, thin and undernourished and visceroptotic in build Tongue was heavily coated and breath fetid Chest was phthisical in type, but lungs clear Heart was normal The lower pole of right kidney was palpable on inspiration Tendon reflexes were all exaggerated

Laboratory studies, including blood count, urinalysis, blood sugar, blood urea nitrogen, basal metabolism, and Wassermann test, were all negative or normal Fractional gastric analysis showed the highest free hydrochloric acid as 22, the highest total acidity as 50

Roentgenological studies of the gastro-intestinal tract re vealed the following important facts Moderate six hour residue with a vertical J shaped stomach Peristalsis at times con siderably more than average in intensity, but at other times

normal, it was of the four-wave type   Motility somewhat less than commensurate   The duodenal cap showed marked dilatation and stasis in the first and second portions, with vigorous antiperistalsis   Serial exposures showed no constant defect, but there was an inconstant defect of the pylorus near the isthmus, suggesting a congenital veil   The summary of the a-ray study was   "Dilatation of the duodenum probably due to ligament of Treitz obstructing the duodenum at the third and fourth portions "

Be ˉuse of the history and these a-ray findings, a diagnosis of chronic duodenal ileus was made, and operation advised At operation by Dr G P Muller, the duodenum was considerably distended, and at the duodenojejunal junction the ligament of Treitz formed such an acute angle in the small intestine that obstruction was almost complete   To relieve this a duodenojejunostomy was performed   The patient made an uneventful convalescence and was discharged in good condition   When seen four months later she was almost entirely free of gastrointestinal symptoms, had gained weight, and was much improved in every way

This patient illustrates well the asthenic, nervous, visceroptotic type of individual so common in this group   It is interesting to note that symptoms of a gastro-intestinal nature were present from childhood, as might be expected in case of a congenital lesion   The vague nature of her complaints might well suggest, at first glance, a functional condition—a diagnosis substantiated by her symptoms of nervousness, palpitation, and sleeplessness   On closer scrutiny, however, most of her symptoms are found to be consistent with those of chronic duodenal ileus Anorexia, headache, fatigability, coated tongue, fetid breath, mental depression, all suggest a process of autointoxication not to be laid too quickly at the door of a sluggish colon, but rather to absorption of toxic products from the higher digestive tract The indefinite nature of the abdominal pain or discomfort is in accordance with the usual story of this toxic group of chronic duodenal ileus cases

Case II.—H S , a white man, twenty eight years of age, stated that he was perfectly well until nine years before his admission to the hospital, September 4, 1928 At that time he developed distress after eating This was described as dull, boring pain located in the epigastrium, coming on about an hour after eating, and relieved by food Eructations were troublesome Soda gave no relief Pain was severe in character for one year, during which time he took as many as 25 morphin tablets by mouth for relief There were on the other hand, intervals of weeks or months when he was entirely free from pain or discomfort In 1923 he was diagnosed as having duodenal ulcer and placed upon a Sippy regimen, but with no permanent relief In 1925 a gastro intestinal x ray was reported as showing duodenal ulcer and surgery was advised but refused After that time up to the date of his admission his symptoms continued unchanged, with the exception of the pain which was described as being definitely less There was no history at any time of nausea, vomiting, melena hematemesis Bowels were reported as constipated There were no nervous symptoms, no headache, and a loss of only a few pounds in weight

Past history was essentially negative as was also his family history save that his mother died of tuberculosis and his father of "gangrene of the bowel " The patient worked as a machinist He used alcohol freely

Physical examination, which showed a man of rather stocky build, was essentially negative except for relaxed inguinal rings (but no hernia) and slight tenderness to pressure in the epigastrium

Fractional gastric analysis showed the highest free hydrochloric acid as 70 and the highest total acidity as 146 Other laboratory studies, including blood count, urinalysis, blood urea nitrogen, and blood Wassermann, were all normal or negative

Roentgenologic studies showed a J shaped stomach with the greater curvature 3 inches below the level of the ileum, and a moderate six hour residue A moderate degree of hyper peristalsis with commensurate motility was observed The duodenal cap varied considerably in size during the examination

and never appeared to be regular in outline The second and third parts were abnormally filled out and at times antiperistalsis was noted Serial exposures showed a constant irregularity of the cap The report was summarized as showing congenital adhesions about the pylorus as well as adhesions about the duodenal bulb which produced a definite obstacle at the junction of the third and fourth portions of the duodenum

Surgery was advised and this time consented to The important findings of the operation are described as follows "There was an extreme degree of visceroptosis, the greater curvature of the stomach reaching practically to the pelvic brim The jejunum was resting on the promontory of the sacrum The pull of the ptosed organs combined with pressure by the superior mesenteric vessels at the duodenojejunal junction were the causes of the partial duodenal obstruction and the coincident dilatation The ligament of Treitz was exposed and severed, although this was not the main cause for the obstruction No ulcer was found either in duodenum or jejunum, and the gall-bladder was normal "

This patient, too, made an uneventful recovery and was discharged from the hospital in good condition When seen about a year later he had gained weight and was much improved, although at times he continued to have some epigastric distress

This case illustrates well the second group of symptoms common in chronic duodenal ileus, i e , the group which suggests organic disease of the duodenum or gall-bladder The patient's boring, epigastric pain coming on an hour after meals, associated with eructations, and relieved by food were certainly suggestive of duodenal ulcer, as were also his intervals of freedom from symptoms, and his first x-ray series However, the severity of pain for which morphin was required, the fact that neither soda nor Sippy treatment gave relief, raised the question of some other pathologic factor

In the series of 40 patients studied, symptoms of both these types were evident Of the symptoms indicative of the toxic group, headache was perhaps the most prominent, 11 out of

the 40 giving a history of severe headache, and 1 of almost constant headache for twenty years. Nine complained also of easy fatigibility and 6 of states of mental depression. Constipation was the rule in the series. Vanderhoof[3] has called attention to the presence of obstinate constipation and headache in this group. Loss of weight was present in 12 of the series, though only 2 had lost as much as the first patient. "Gas on the stomach" eructations, and abdominal pain or discomfort of a vague nature were common complaints in the toxic group. It is interesting to note in connection with the first patient, that although gastro intestinal symptoms were present from childhood, she coped fairly well with a congenital lesion until she suffered a general breakdown. Wilkie[4] and other writers have postulated theories to explain why such congenital abnormalities give rise to symptoms only in adult life. In our series several patients gave a history of straining at onset of symptoms (as childbirth, lifting heavy weights, etc)

Of the symptoms suggestive of organic disease, pain was perhaps the most important. The nature of the pain in our series varied from a dull ache to a sharp stabbing pain, 10 describing it as dull and aching, 17 as sharp and severe. Figures on this point are misleading, however, for several types of pain occurred in the same individual at different times. Fifteen described the pain as coming on from one-half to two hours after meals, the others had no time relation to food. Most cases obtained little or no relief from food, 8 gave a history of relief by food or alkali, but several of these stated that this was true only in the beginning. In location, pain was by no means confined to the epigastrium, but was described as being in the right upper quadrant, the left lower quadrant, the epigastrium, and even the lumbar regions, 16 locating it in the epigastrium. Periodicity of symptoms was not a feature in our cases, it being present in less than half of them. Harris[4] also found on analysis of his cases that there was an absence of marked intermissions and bad relapses as in ulcer cases. The absence of nausea, vomiting, melena, hematemesis, as noted in the second case, is more consistent with a diagnosis of chronic

duodenal ileus than of duodenal ulcer   Twelve of our patients complained of nausea and 7 of vomiting, none of hematemesis, 1 of passing blood by bowel (Case I)   Wilkie,[5] Leveuf,[6] and others state that the presence of crises of vomiting bile-stained fluid is necessary to the diagnosis of chronic ileus, this is at variance with the observations on our small groups

Physical examination, as in both these patients, was uniformly unimportant save for revealing the ptotic habitus in most, though not in all, of the 40 patients   Laboratory studies were likewise unimportant, except for gastric analysis   The first case presented showed normal acid figures, the second, figures above normal, the hyperacidity substantiating the diagnosis of duodenal ulcer   In general the acid figures of the group were normal or slightly above normal   Hyperchlorhydria was not found to be the rule, as in Harris' cases   Three cases in the series showed no free hydrochloric acid and a low total acidity   Subsequent examination of these, however, reported plenty of free acid in 2, but the third remains recorded as an achlorhydria

In both of the cases presented the diagnosis was made by means of careful roentgenologic studies   These are of the greatest importance, for the diagnosis is so made in most instances   Leveuf,[6] Cole,[7] and others have laid down criteria for such Roentgen-ray diagnosis   The chief of these are (1) dilatation and stasis in the duodenum with slow emptying of stomach and duodenum, (2) antiperistalsis, and (3) sometimes constant deformity of the duodenal cap   Twenty of the 40 cases studied had such constant deformity

Of the 2 cases presented 1 is a woman and 1 a man, in our series 22 were women, 18 men   The woman's age is given as thirty-three years, the man's as twenty-eight   The more advanced age for the woman is in accordance with the general data of our group in which the age of the women seeking treatment is about a decade later than that of the men   Both seek treatment in early adult or middle life

The first case was found at operation to be suffering from partial obstruction due to a congenital membrane (ligament

of Treitz), the second case to compression of the duodenum by traction on the mesenteric pedicle These are illustrative of the two pathologic states which operate to produce chronic duodenal ileus

Medical treatment may be tried in these cases when surgery seems inadvisable. Such treatment consists of small frequent feedings of high caloric value, rest in bed with the foot raised, duodenal lavage, abdominal support knee-chest posture etc Such treatment is often helpful but requires considerable perseverance on both the patient's and the doctor s part Surgical treatment is more hopeful Most surgeons are content to sever adhesions as was done in the second case Duodenojejunostomy, however although still considered a somewhat formidable procedure for a patient suffering "only from adhesions," is probably the operation which gives best results Barker[8] in 1906 was the first to suggest this method of relief, and Stavely[9] in 1907 the first to perform it In the past ten years numerous reports of duodenojejunostomy have appeared in the literature Notably among these are those of Wilkie,[10] who up to 1927 had performed 64 duodenojejunostomies for ileus, and those of Kellogg and Kellogg,[11] who in 1926 reported 118 duodenojejunostomies alone or in combination with other operations Of the 2 cases presented here both, seen some months after operation have gained weight and admit improvement The first case is almost entirely free of gastro-intestinal symptoms and is rapidly being reinstated as a useful member of society The second case has gained about 15 pounds in weight and is considerably better as to symptoms, but at times continues to have some epigastric distress This possibly is an argument in favor of the more radical surgical procedure performed in the first case

To reiterate in conclusion these 2 cases of chronic duodenal ileus are presented in conjunction with the observations on a group of 40 such cases studied in an effort to define more clearly the symptomatology of this group

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PURPURA, WITH PARTICULAR REFERENCE TO ESSENTIAL THROMBOCYTOPENIA (PURPURA HEMORRHAGICA)

I WISH to take up with you today the condition known as purpura, characterized by hemorrhages under the skin and mucous membranes With the advent of more accurate methods for counting blood platelets, and a clearer understanding of their physiology, a working classification of purpura is possible The following is an outline of Leschke's classification

1 Essential thrombopenic purpura (essential thrombopenia, essential thrombocytopenia, purpura hemorrhagica, morbus maculosus Werlhofu

2 Symptomatic thrombopenic purpura

    (a) Blood diseases such as leukemia, pernicious anemia, aplastic anemia, hemolytic jaundice, Gaucher's disease, carcinomatosis of the bone marrow, lymphogranulomatosis

3 Non thrombopenic purpura

    (a) Anaphylactoid purpura (Schönlein's Henoch's)

    (b) Purpura simplex

    (c) Avitaminosis (scorbutus, Barlow's disease)

    (d) Capillary weakness (purpura senilis, cachexia)

    (e) Infection (bacterial capillary emboli, toxic capillary, in septic disease)

This classification brings two diseases, namely, Henoch's purpura and Schönlein's purpura (purpura rheumatica) under the one heading, anaphylactoid

It emphasizes the importance of blood platelet study and draws attention to the importance of infection as an etiologic factor in purpura

However, as I will show later, it is not always possible to place all cases of bleeding in these groups

The subject of purpura is too large to deal with in one clinic and I wish to direct your attention to the group number one—essential thrombopenia or purpura hemorrhagica

Etiology —The cause of this condition is not known Disturbances in capillary endothelium has been given by many observers as the main etiologic factor—as you know, the blood-plates are greatly reduced in this condition and Hayem, Frank, Brill, Duke, and others feel that this is the chief factor in its production Personally, I have never felt that this view was entirely correct Some of you recall seeing the young man of eighteen years with petechiae and epistaxis whose blood-plates were always between 150,000 and 250,000, and I have previously spoken of the woman with blood-plates between 75,000 and 90,000, who did not show any hemorrhagic phenomena at that time The belief held by others that both platelet reduction and capillary dysfunction are responsible, is more tenable One must look further, however, for the cause of these two disturbances It is not improbable that the capillary endothelium is inherently weak in certain individuals and that plates are more easily destroyed, less resistant, in others

A third factor, I am convinced, should be added and that is infection—chronic, focal, and acute We know that in small-pox, scarlet fever, typhoid, streptococcic septicemia, and bacterial endocarditis, hemorrhagic phenomena occur The exact mechanism of production is unknown, but it may result from capillary dysfunction, thrombopenia, and splenic injury

A fourth factor, really a subhead under the third, is that of direct injury to the mucous membrane—one of your classmates, you will recall, suffered from severe hemorrhage from the bowel, following a nasal operation The nasal and pharyngeal mucous membrane became very fragile and bled with the slightest irritation, a streptococcus was isolated He recovered after a series of transfusions and the x-ray by Dr W F Manges failed to show any gastro-intestinal pathology Furthermore, he has

been perfectly well ever since   Just this Monday a boy of
five years, a patient of Dr Stroup's, presented a similar symp-
tom-complex, namely, severe streptococcic infection of throat
and nasal mucous membrane with bleeding from the bowel,
and in this case epistaxis   The mucous membrane had much
the same appearance as that of the student   Recently Dr
Vonglahn, of the Presbyterian Hospital, demonstrated a phlegmon
of the duodenum with streptococcic infection of the mucous
membrane—I spoke to you some time ago about the patient
who had nasal hemorrhage at intervals for forty four years
whose nasal mucous membrane Dr Warren Davis found to be
swollen, grayish, and easily made to bleed   This patient also
had blood in his stools, the x-ray revealed the presence of a duo-
denal ulcer which Dr Gibbon found at operation to be of the
chronic penetrating type

Infection, acute, chronic or focal, directly or indirectly influ-
encing capillaries and mucous membranes and spleen, inherent
capillary weakness, making the cells more liable to injury, de-
ficient blood platelet formation or greater platelet destruction
seem to be the factors in the production of typical and atypical
purpura

Methods of Diagnosis —Blood plates are counted by the
method of Reese and Ecker, using a solution of brilliant cresyl
blue, 1 gm , formalin 2 c c , sodium citrate 3 5 gm   Draw the
solution in the red cell tube to 0 5 and then blood to 1 and so-
lution to 1 01, mix and place on counting chamber for ten
minutes and count all the plates in 400 squares, multiply by
2000 to obtain the total number   It is important to draw the
blood into the tube as soon as the second drop appears

Blood platelets number normally from 300,000 to 400,000
per c.mm. More than 450,000 is considered an increase and less
than 250,000 a diminution   They may be 10,000 or less in
thrombocytopenia and usually are between 40,000 and 70 000
in the acute cases

Bleeding Time (Duke) —Make a puncture 4 mm deep with
a sharp plunger, at first appearance of drop, note time   As
soon as blood appears blot, do not rub, when blood no longer

appears, the bleeding time is taken, normally this is one to three minutes In purpura, it may be greatly prolonged

Clotting Time —This may be done by the capillary-tube method, using the 1 mm tube and is usually within normal limits or slightly prolonged   Two to seven minutes is normal, if this tube is used

Clot Retraction —Take 2 to 5 c c of blood in test-tube and let it stand   In purpura hemorrhagica, the clot, although firm, does not retract and extrude the serum

Capillary Resistance Test —In many cases of purpura hemorrhagica, a tourniquet placed around the arm for three to five minutes, not entirely obliterating the pulse, results in the appearance of petechiæ above and below the tourniquet

Trauma Phenomenon —Strike sharply over the sternum or tibia with a rubber percussion hammer and in a few minutes a readily palpable indurated area will appear beneath the skin Later this becomes a hematoma

Hess Puncture Test —The subcutaneous injection of $1\frac{1}{2}$ c c of 0 2 per cent NaCl solution results in the formation of a hematoma

Reticulocyte Count —Brilliant cresyl blue, 0 26 gm in 100 c c of 96 per cent alcohol, makes up the reticulocyte stain   A clean cover-glass is covered by this stain   The blood-smear is made directly on the dried stain   Enumerate all the reticulocytes seen in counting 1000 red blood-cells   In purpura hemorrhagica, these cells are usually increased above the normal of 1 to 2 per cent , and sometimes are found in numbers as great as 50 per cent

Complete Blood Count —The white blood-cells are a high normal or increased   The differential count is either normal or there is a polynuclear increase, nucleated reds often are numerous

Van den Bergh Test —This test is negative, both direct and indirect

Fragility or Red Cell Resistance —The resistance of the red cells to saline dilutions is within normal limits, namely, 0 42 to 0 34 per cent

Icterus Index —The icterus index is normal between 7 and 9 units

Diagnostic Points of Importance —1 Hemorrhage from the lung is almost unknown

2 The purpuric and ecchymotic spots are most numerous on the dependent portions of the body

3 The spots at first are bright red and then purple

4 They do not fade on pressure

5 The hemorrhage into mucous membranes may distend them, but the gums are not spongy

6 Arthritis is rarely present

7 Urticaria and erythema are absent

8 Lymph nodes are not enlarged

9 The hemorrhage is spontaneous, a history of injury is seldom obtained

10 The spleen may or may not be palpable, but is rarely large

Differential Diagnosis —It is of great importance to the patient to make the diagnosis of purpura hemorrhagica, especially in the fulminating cases, because active treatment may bring about a cure Aplastic anemia and acute leukemia may be seen first during a hemorrhage from mucous membranes, and in those conditions the outlook is hopeless

In *aplastic anemia*, even though the bleeding time is long, the plates are greatly reduced, the capillary resistance test positive, there is a marked leukopenia, and the polynuclear percentage is low, the reticulocytes reduced or absent, the nucleated reds absent, and the bone-marrow aplastic

In *leukemia* the differential count is sufficient to establish the diagnosis, even though glandular enlargement may be absent

Hemophilia is often mistaken for the more chronic forms of purpura hemorrhagica and even for the fulminating type In hemophilia, the plates are formed in normal numbers, the bleeding time is normal, the clotting time greatly prolonged the capillary resistance test negative, and there is a definite family history of bleeding

Scurvy is characterized by a brawny hemorrhagic infiltration of the thigh or lower leg, and by spongy gums In purpura

the small petechiæ are rarely found about the hair follicles, and the gums rarely become greatly swollen and spongy   The plates are not reduced in scurvy

In *anaphylactoid purpura*, hemorrhage from mucous membranes is unusual, but may occur   The erythema, the joint involvement, the normal bleeding time, and platelet count help to establish the diagnosis   Other blood diseases as Addison's anemia, Gaucher's disease, purpura simplex, Hodgkin's disease with purpuric manifestations may be confused with the subacute or chronic form of essential thrombocytopenia   Careful attention to the special methods of diagnosis will make the differentiation possible in the majority of instances

This patient, Evelyn, is twelve years of age   Three years ago she had frequent nosebleeds, vomited a large amount of clotted blood, and had frequent tarry stools   Petechiæ and ecchymosis were present on the extremities and in the mouth   The spleen was palpable   She was admitted to the private ward on April 8th with hemoglobin, 45 per cent , red blood-cells, 2,680,000, white blood-cells, 8200, polynuclears, 54 per cent , lymphocytes, 40 per cent , mononuclears, 6, bleeding time, sixteen minutes, two seconds, clotting time, three minutes, twenty-five seconds, bloodplates, 10,000, fragility normal

Dr Lott controlled the nasal bleeding by applying, loosely, cotton pledgets saturated with thromboplastin   Four whole blood transfusions were administered, April 10th, 140 c c , April 14th, 160 c c , April 20th, 120 c c , April 24th, 120 c c

Blood Counts —

	Hgb	R B C	W B C	B T	C T	Plates
April 12th	58	3,000,000	7200	10' 20"	2'	15,000
April 15th	62	3,420,000	6800	8'	2' 30"	16,000
April 21st	70	3,900,000	7400	5' 20"	2' 20"	18,000
April 25th	80	4,180,000	8200	4' 20"	3'	32,000
April 27th	82	4,200,000	7000	6' 40"	3' 5"	86,000
May 20th	95	4,810,000	7600	3' 50"	3' 75"	186,000

An ounce, repeated in a half hour, of the fluidextract of Ceanothus americanus (Ceanothyn) was administered by mouth

As soon as the patient could eat she was given foods that were

finely divided with special emphasis placed on those high in vitamins B and C

Splenectomy was advised, but her mother refused to permit operation   Three years have elapsed since the hospital admission The first year ultraviolet therapy was employed once or twice weekly   30 inches for two minutes   Her mother placed her on a farm where she had an abundance of fresh fruits and vegetables and could lead an outdoor life

Blood studies have been made at intervals, the platelet count has never been below 200,000 nor the bleeding time greater than five minutes   At present the hemoglobin is 90 per cent, red blood-cells, 4,860,000, white blood-cells, 7000, bleeding time, three minutes, forty seconds, clotting time, four minutes, platelet count, 420 000   Her mother states that on several occasions a few petechiæ have appeared on the legs and once she had a slight nosebleed   Otherwise, she has been in perfect health

It is of interest to note that her brother of six years has had petechiæ at intervals and on one occasion developed a fairly marked secondary anemia with plates of 140,000 and bleeding time five minutes, forty seconds   We are unable to find evidence of mucous membrane bleeding   He has been benefited by his outdoor life

Other Forms of Treatment
    1   Medication
    2   Ultraviolet ray and diet
    3   x Ray
    4   Transfusion
    5   Splenectomy

The Acute Fulminating Type —In the acute fulminating form blood transfusion must be used to the exclusion of all other forms of treatment   The blood should be undiluted and in amounts large enough to relieve the urgent symptoms   To one patient we gave three transfusions in thirty six hours   After the acute stage the transfusions should be given at three- to five-day intervals until the blood reaches 70 per cent of normal, at which time splenectomy should be advised

    1   Medication is of value in the subacute or chronic forms

It consists chiefly of substances supposed to influence the bleeding Para-thor-mone in 20- to 30-unit doses hypodermically, repeated in thirty-six hours, has had deterrent effect on the bleeding Ceanothyn given by mouth in the dose of 1 ounce, followed by a second ounce in one-half hour, has reduced bleeding time in several patients—it is harmless and can be repeated every eight hours

One of our most useful methods is the injection intramuscularly of 20 to 30 c c of whole blood This may be given daily Not only does it affect the bleeding but also stimulates red cell increase The older clinicians used oil of turpentine, 10 to 15 minims, three times daily, and claimed that excellent results were obtained

Dr Fitz-Hugh and I have noticed the increase of platelets in purpura following the ingestion of liver extract, although there was a failure of effect in the last case in which I used it

2 Sooy and Moise have reported a series of cases in which the ultraviolet ray treatments resulted in the disappearance of symptoms and an increase in plates and other blood elements As I have pointed out previously many of the cases of thrombocytopenia have seasonal variations very much like pernicious anemia This is one reason for the use of liver extract and for a similar reason, fresh fruits, vegetables, and out-of-door life are indicated

3 Pancoast found x-ray to the spleen and over the long bones to be of great benefit This treatment may be utilized by those experienced in x-ray work, but if improperly administered a severe bone-marrow depression may result

4–5 I have already spoken of transfusion Many of the subacute and chronic cases require blood before splenectomy can be performed safely Splenectomy is contraindicated in the acute fulminating variety, but in the subacute and chronic types the results are very satisfying You will find, however, that many of the patients refuse the operation and it is necessary to carry on with treatment such as I have just outlined

Many of these patients may be carried along for years to what seems to be a permanent cure I know of 2 patients who

had acute attacks of the disease, one forty five years ago and the other twenty five years ago Both are in good health today and have not had an attack since that time Dr Alfred Stengel saw this latter case in consultation and made the diagnosis

This disease is as interesting as it is complex Much can be done for these patients if the treatment is timely, active, and persistent Take time to make the correct diagnosis so that none of your patients who have this disease dies because of a diagnosis of acute leukemia and because little effort is made to save them Finally, consider well the etiologic possibilities, with the hope that some of you may make it possible to remove from that great list of blood diseases one, of which we may say, the cause is known

ALLERGIC CLINIC OF DR HARRY B WILMER

GERMANTOWN AND PRESBYTERIAN HOSPITALS

INTERESTING OBSERVATIONS IN THE DIAGNOSIS AND TREATMENT OF THE ATYPICAL TYPES OF HAYFEVER

IN reviewing approximately 1900 cases of hay fever, I have been able to classify a number of these which I will consider atypical in type Much has been written on the treatment and diagnosis of the typical cases but little has been seen in the literature on the unusual cases I, therefore, thought it might be of interest to this society to hear of our findings I will endeavor to present the subject in the following manner

1 The cases having definite hay fever symptoms with no positive skin or conjunctival tests It has been my experience that these types of cases may be divided into two types those having no skin sensitivity, and those suffering at the time of testing with some acute constitutional condition with fever The latter type is given instructions to return after all fever has disappeared for further testing when a positive test is seen and proper treatment is instituted In the former a positive test may never be seen and, in consequence, if the symptoms are conclusive as to the time of pollenation, treatment may be instituted with the commoner pollens, pollenating at that time, with safety

Of the former type we had 44 cases, with the following results

No of Cases	Cured	Improved	No Relief
44	15	17	12

2 The cases having definite asthma, with no hay fever symptoms, occurring in the hay fever season

Here we may have two types, those showing positive skin tests, and those showing no skin tests

Those showing positive skin tests the diagnosis is easy and proper treatment may be given, with good results But, in those with no skin tests, the same method is used as in paragraph No 1

Of these types the following table will show the results

Hay-fever Asthma with Positive Skin Tests

No of Cases	Cured	Improved	No Relief
30	15	10	5

Hay-fever Asthma with No Skin Tests

No of Cases	Cured	Improved	No Relief
10	5	0	5

3 Cases with marked bladder tenesmus and frequency of urination, occurring in the hay-fever season, and showing positive skin reactions

Institution of proper desensitization and removal of all uncooked vegetables show the following results

No of Cases	Cured	Improved	No Relief
2	2	0	0

4 Cases with general eczema of the body with negative tests to all proteins except pollens, and with no hay-fever symptoms

Desensitization with pollen extracts was instituted with no relation to seasons, with the following result

No of Cases	Cured	Improved	No Relief
4	3	0	1

5 Cases showing a marked dermatitis, grading from a mild erythema to a pustular eruption, with positive skin tests to the pollens and no hay-fever symptoms

There were 4 cases of this type seen, 2 reacting to ragweed, short and long, and 2 reacting to Timothy pollen Desensitization was instituted in 2 of the cases during the season, with decided relief, and all 4 received ultimate preseasonal desensitization, with the following results

No of Cases	Cured	Improved	No Relief
4	3	1	0

6 Cases showing positive skin tests and having typical hay-fever symptoms, treated preseasonally by the long interval method, which gave no relief at all, were, the following year, treated by the short interval method, receiving an injection daily for two weeks, and then an injection once weekly for the entire season, showed the following results

No of Cases	Cured	Improved	No Relief
25	15	4	6

7 Cases having definite attacks of hay-fever all the year round, with positive skin tests to the pollens These cases had been diagnosed vasomotor rhinitis On close study we were able to prove without doubt that these patients were, from time to time, coming in contact with pollen which had been harbored from the season before in books, floor coverings, and leaves banked in protected spots near the living quarters of these individuals

8 Cases with persistent asthma hay fever, and positive skin tests, who have been treated with pollen extracts alone and in whom no relief has been derived from the treatment. The addition of an autogenous bacterin with the desensitization, shows the following results

No of Cases	Cured	Improved	No Relief
40	20	5	15

9 Cases with typical hay-fever symptoms and negative skin tests except for reaction to one pollen of unusual origin

In this type of case only by an exhaustive study of the plant life in the environs of that particular person, and by proper isolation of the pollen, and by proper desensitization with that pollen, can a cure or relief be hoped for

10 Cases so frequently diagnosed vernal conjunctivitis

In these cases there may or may not be, and in the majority of cases, there is no positive skin test, but there may be a positive conjunctival test   It has been our experience, in the 10 cases seen, there was a staphylococcic infection also present, and a bacterin was made and given in conjunction with the proper pollen combination

It must be borne in mind that these cases are always seen early and during the time of tree pollenation   Many reactions are extremely slight, but should be considered as a cause

No of Cases	Cured	Improved	No Relief
10	7	2	1

MENINGOCOCCIC (LATER ALSO STAPHYLOCOCCIC) MENINGITIS, LOW SPINAL SUBARACHNOID BLOCK, ABSCESS, LAMINECTOMY, RECOVERY

Case Report—This boy of fourteen, who now appears normal in all respects, was admitted to Medical Service "B" nine months ago with meningitis Five days prior to his admission to the hospital, he was awakened from sleep by nausea He vomited several times and, on the following day, he appeared feverish and again vomited Two days later his throat became sore a rash appeared upon his body, and the joints of his fingers, wrists, elbows, knees, and ankles became swollen, red, and painful On the day before admission he became delirious

Examination showed a very ill boy lying on his side, delirious, with head drawn back and knees flexed The joints of the knees, ankles, left elbow, and fingers were swollen, red, and tender Because of pain no attempt was made to elicit Kernig's sign There was a slight strabismus at times, which produced an intermittent diplopia The throat was injected, and the entire body, including the face, was dotted with a maculopetechial eruption A blood count showed a leukocytosis of 19,000, with 84 per cent polymorphonuclear neutrophils present, and normal figures for the hemoglobin and erythrocytes The blood sugar was 140 and the blood urea nitrogen 26 mg per 100 c c A blood-culture was negative An uncatheterized sample of urine had a specific gravity of 1 012, and contained many bacteria, but was otherwise negative The respiratory rate was 22, the pulse and temperature are shown on the accompanying graph Throughout both lungs rales were heard The heart

was regular and no adventitious sounds were heard   The abdomen was moderately distended and tympanitic   A lumbar puncture was immediately done, and purulent fluid was secured under 17 mm pressure, which with jugular pressure rose slowly to 22 mm   After 15 c c of spinal fluid had been removed no more could be secured from the needle   Ten c c of antimeningococcic serum was then injected and the spinal fluid taken to the laboratory for examination   It was reported to contain 1180 leukocytes per cubic millimeter, 45 per cent of which were lymphocytes and 55 per cent polymorphonuclear leukocytes   A smear showed a few intracellular diplococci, which were later identified by Dr C Y White as meningococci   Later in the day a combined lumbar and cisternal puncture was done   The cisternal fluid was less purulent than that obtained by the lumbar puncture, both fluids contained 20 mg of sugar per 100 c c   When serum was introduced into the cisterna it produced an accelerated flow of fluid from the needle in the lumbar region, but when its introduction was discontinued the flow from the lumbar needle diminished

On subsequent days the introduction of serum was continued either by the lumbar or cisternal route as is shown in the graph (Fig 171) on page 1053, and the patient's condition gradually improved   On the fourth day after the patient's admission to the hospital a crop of herpes appeared about his mouth and ears, and on the eighth day an urticarial eruption made its appearance, but the administration of serum was continued His general condition seemed improved and he was no longer delirious   This improvement, however, gradually gave way to an exacerbation of symptoms, and he complained of generalized pains and hyperesthesia   The lumbar and cisternal puncture fluids on the eighteenth day showed a growth of Staphylococcus aureus   Smears of both cisternal and lumbar puncture fluids contained meningococci and showed 95 per cent of polymorphonuclear leukocytes and 5 per cent lymphocytes to be present Cell counts could not be made because the lumbar puncture fluid was too thick and the cisternal fluid contained blood Sugar was reported as absent in both fluids   The pains became

GRAPH OF CASE WITH MENINGOCOCCIC LATER STAPHYLOCOCCIC MENINGITIS
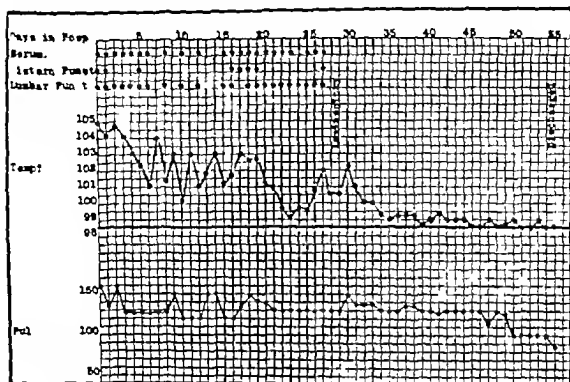LOW SPINAL SUBARACHNOID BLOCK AND ABSCESS FORMATION RECOVERY
FOLLOWING LAMINECTOMY

Fig 171 —Condensed temperature and pulse record highest tempera
ture and pulse-rate being given for each day In all 348 c c. of antimenin
gococcic serum was administered mostly in 15 c c. doses by lumbar and cis-
ternal routes on days shown above Staphylococcus aureus vaccine was also
administered daily from the thirty third to the thirty ninth day in doses in
creasing from 2 000 000 to 200 000 000 killed organisms and from the thirty
ninth to the fifth third day on alternate days in doses of 200 000 000 killed
organisms

localized more in the legs and the patient became irrational
again Ophthalmologic examination showed optic neuritis
Strabismus was continuous and the neck was rigid and retracted
On the twenty fourth day a small circumscribed area of infec
tion was noted at the lumbar puncture site An x ray of the
spine was made for evidence of osteomyelitis but this was nega
tive The lumbar puncture fluid became thicker from day to
day, and on the twenty seventh day signs appeared of complete
subarachnoid block at some point between the cisternal and
lumbar puncture sites The cisternal pressure was 22 mm
and rose to 26 when jugular pressure was practiced but neither
jugular pressure nor the introduction of fluid into the cistern

produced any change in the lumbar puncture pressure, which was 20 mm   The cisternal puncture fluid appeared clearer than on previous occasions and contained approximately 50 cells per cubic millimeter, with lymphocytes predominating, and on culture again yielded the Staphylococcus aureus   Lumbar puncture yielded a purulent exudate so thick that no cell count could be made   Smears showed diplococci and culture yielded the Staphylococcus aureus

An examination by Dr Fay of the Neurosurgical Service, showed hyperalgesia in the sacral and first two lumbar skin segments, absence of the Achilles and patellar tendon reflexes on both sides, and marked tenderness to pressure over the nerves of the lower extremity   Babinski's sign was negative, and there was present neither clonus nor paralysis   There was retention of urine and partial loss of anal sphincteric control These findings together with the results which had been obtained by lumbar and cisternal puncture, were interpreted as indicating a subdural or extradural abscess, extending as high as the second lumbar root of exit   An operation at the level of the third lumbar lamina was advised

Operation —On the twenty-eighth day after the patient's admission to the hospital, Dr Fay performed a laminectomy of the third lumbar vertebra under ether anesthesia   There was no extradural collection of pus   The dural sac was bulging and tense   Upon opening the dura the nerve roots of the cauda equina were found matted together by the products of recent inflammation   No pus was obtained   The nerve roots were separated and a hemostat introduced 1 cm into the dural sac without obtaining pus   The opening was then carried further caudally, and 30 to 40 c c of pus escaped from the central portion of the sac, the wall of the abscess contained the matted cauda equina roots   A two-way drain was placed in the abscess cavity and the tubes brought through the dura to the skin surface   Irrigation with warm saline solution through one tube gave free escape and drainage from the other   The dura was left open, the muscle layer and skin being closed by four approximating sutures

From this time forward the patient's condition began to improve. The wound drained freely and was irrigated five times daily with Dakin's solution. The tubes were allowed to remain in situ until the irrigations became clear, they were then removed. The wound healed by primary intention leaving a small sinus.

An examination made by Dr. Gotten of the Neurosurgical Service two weeks after the operation showed "neuroretinitis in both eyes, weakness of the external rectus muscle of the right eye, pupils widely dilated but react to light and accommodation. The other cranial nerves are normal. The biceps, triceps, abdominal, corneal, cremasteric, patellar, and Achilles reflexes are active and equal. Babinski's sign is negative. Vibratory and touch sensation are normal over the entire body. Motor power is diminished about 25 per cent over the entire body with the exception of the right leg which is spastic, and has a diminution of about 50 per cent in its motor power."

On the fifty fifth day after his admission he was discharged in good condition except that the sinus remained unhealed, and there was some weakness of the right leg. The sinus continued to discharge slight amounts of pus until some months later when following the removal of a small piece of bone and an unabsorbed suture from the sinus by his family physician the sinus healed. An x ray shows the posterior spinous process of the third lumbar vertebra to be absent but is otherwise negative. He walks well, looks well and has no complaints. A neurologic examination by Dr. Fay is completely negative.

Discussion.—I wish to draw your attention to the complications presented by this case. The rash and the herpes are such frequent accompaniments of meningococcic meningitis that they only deserve to be called complications when they present unusual and severe manifestations as for example, when the herpes is widespread and zoster like in its distribution. The ordinary forms of herpes vary in frequency of occurrence appearing in 90 per cent. of the cases in some epidemics while in others herpes is seldom noted [1]. The rash of meningitis varies similarly in its incidence being frequent in some epidemics and

rare in others   its presence is determined, according to some observers, by the particular type of meningococcus encountered

Joint involvement, an outstanding complication of this patient's early illness, may be expected in from 10 to 15 per cent of cases, and may range from a mild arthralgia to a severe and sometimes purulent arthritis   Like the skin eruption, it may be regarded as a septicemic manifestation of the meningococcic infection, and therefore comes most frequently in the early stages of the disease before the organisms have become localized in the meninges

The case before us presented two ocular complications—optic neuritis and strabismus   The former, according to Netter and Debré[2] is quite common, appears early in the disease and is to be regarded not as an evidence of intracerebral pressure but as a perineuritis of the optic tract, or an "optic meningitis"   Squint occurs in from 10 to 25 per cent of cases, and usually, if at all, in the first week of the disease   In this respect it differs from the strabismus encountered in tuberculous meningitis, which, if it occurs, is generally a late manifestation   This point may aid in differentiating these two forms of meningitis

Secondary infection of the meninges whether it occurs spontaneously, or due to an error in technic, is a rare complication of meningococcic meningitis   It may be expected in about 1 5 per cent [3, 4] of cases, and is generally due to the pneumococcus   In the present case, after the eighteenth day in the hospital, Staphylococcus aureus was repeatedly recovered from the fluid obtained by lumbar and cisternal puncture   It is strange that secondary infection should not be more common, since it has been shown in experimental animals that lumbar puncture following the intravenous injection of living organisms usually resulted in meningitis, while controls who received the same or double the dose of organisms intravenously without the lumbar puncture failed to develop meningitis [5]   When secondary infection of the meninges occurs in a case of meningococcic meningitis it is usually a fatal complication

The fluid obtained by lumbar puncture in the present case was purulent from the first, and contained a higher proportion

(45 per cent) of lymphocytes than is to be expected at the height of the disease. It is noteworthy that in the early and also in the late stages of meningococcic meningitis the lymphocyte counts are relatively high,[6] whereas the polymorphonuclear leukocytes usually predominate (95 to 100 per cent) at the height of the disease. The fluid obtained by lumbar puncture in this case was repeatedly more purulent than that from the cisterna. Whether this difference was due to a tendency of the leukocytes to gravitate to the more dependent positions of the subarachnoid space or to a more severe involvement of the lower meninges or whether its explanation is to be found in the physiologic factors governing the circulation of the spinal fluid I am unable to say. However, on and after the twenty seventh day, the difference between the cisternal and lumbar puncture fluids became so striking that it could not be explained on any other basis than spinal subarachnoid block.

The commonest site of "block" is at the foramina of Magendie and Luschka,[7] the obstruction of which produces internal hydrocephalus, less commonly blockage occurs within the subarachnoid space of the cord. The tests of Queckenstedt[8] and of Ayer[9] are of especial value in diagnosing these obstructions. The former test can be done routinely in performing lumbar puncture, and consists in exerting sudden pressure or constriction upon the neck on one or both sides, thus producing a congestion of the blood vessels of the brain with consequent displacement of the fluid within the ventricles. If there is no obstruction, the fluid is quickly forced through the foramina of Magendie and Luschka into the subarachnoid space of the cord which under normal conditions, in less than a second, communicates the increased pressure to the manometer connected with the lumbar puncture needle. Release of pressure upon the neck quickly results in fall of spinal fluid pressure where no obstruction exists. In cases of obstruction the changes resulting from compression of the neck are absent, diminished or delayed. Ayer tests for spinal subarachnoid block by performing simultaneous lumbar and cisternal punctures and noting "(a) pressure relations in the two loci, especially changes in pressure which result after with

drawal of fluid, (b) variations in the normal oscillatory movements of the fluid, dependent on the cerebral pulse and respiration, and (c) gross changes in fluid pressure caused by compression of the jugular veins, and by coughing, all indicative of mechanical interference with the continuity of the spinal fluid column " He also notes the physical and chemical differences of the fluids obtained from the two puncture sites In the case before us the thick purulent character of the spinal fluid obscured somewhat the results of these tests, but until the twenty-seventh day the sluggish response to jugular pressure was interpreted as due to the viscid character of the spinal fluid rather than to an actual obstruction to its circulation An x-ray of the spine following the injection of lipioidol[10] or air, might have given further confirmatory evidence of blockage, but inasmuch as it was thought that the viscid character of the spinal fluid might interfere with these tests also, they were not done After the twenty-seventh day the clinical evidences of block in this case were definite these evidences consisted in (a) no rise in the lumbar puncture pressure following jugular pressure, (b) no rise in the lumbar puncture pressure following the introduction of serum into the cisterna magna, (c) an increasing divergence in the character of the fluids obtained by the lumbar and cisternal puncture, the former becoming progressively more frankly purulent, while the latter became progressively clearer Neurologic evidences of involvement of the cauda equina were also present

The operation revealed blockage in an unusual site The cervical or lumbar enlargements of the cord are the sites at which subarachnoid spinal block might be expected, since here a narrower space between the cord and its bony canal exists In this case however the obstruction occurred in the widest portion of the subarachnoid space which ordinarily contains only the nerves of the cauda equina and spinal fluid, and for this reason is the site chosen for lumbar puncture

A search of the literature upon spinal subarachnoid block and allied conditions including abscess of the spinal cord[11] and inflammations of the spinal epidural space[12] has brought to

light one case similar to this one This was reported by Osler,[12] and was that of a sailor aged twenty five who after arthritic manifestations developed the characteristic features of meningococcic meningitis Lumbar puncture yielded thick creamy pus containing diplococci Retention of urine and paralysis of the lower extremities then made their appearance, and a laminectomy was performed by Dr Cushing, a large amount of purulent exudate being drained away Cultures made from the fluid obtained by lumbar puncture and at operation grew the Staphylococcus pyogenes aureus It is concluded from the history and symptoms of the case that it was one of cerebrospinal fever, subsequently infected with the staphylococcus The case before you is in all probability another one of the same nature Although judging from the literature, spinal subarachnoid block in the position which we found it in this case would appear to be of rare occurrence, yet I suspect that it is by no means as rare as one would be led to suppose Lévy[14] in 44 autopsies found purulent collections predominantly at the site of the cauda equina in four instances, and it is well known by pathologists[15, 16, 17] that inflammatory exudates are commonly found at the lowermost portions of the subarachnoid space in meningitis For this reason, one should be led to suspect abscess formation at the caudal end of the dural sac in any case of meningitis developing signs of spinal subarachnoid block, together with involvement of the cauda equina or conus medullaris The case before you emphasizes the importance of recognizing and properly treating such an abscess It should be remembered, however, that hyperesthesia and pain in the extremities are commonly present in uncomplicated meningitis[18]

As regards the treatment of meningococcic meningitis, one need hardly today emphasize the importance of prompt and adequate treatment with a potent polyvalent serum If the disease is suspected, lumbar puncture should be performed immediately, a tube of warm serum being held in readiness to be injected if cloudy fluid is obtained Until proved otherwise, such a case should be treated as one of meningococcic meningitis, notwithstanding negative cultures and smears Repeated search

for the organisms by culture and on cover-slip preparations yields positive results in about 80 per cent [4] of cases, cultures alone being positive in about 50 per cent   In the hands of various workers[19] the mortality with serum treatment is about 26 per cent while without serum it is about 67 per cent

Theoretically, early in the disease the cisternal route should be chosen for the administration of serum   Dr Reilly,[20] of the Pediatrics Division of this hospital, and Ayer[9] have each reported a case treated in this manner   It is possible that the routine employment of this method of treatment may some day find universal employment with the consequent lowering of the present 26 per cent mortality As far as I am aware, however, a sufficient number of cases has not yet been treated by this method to warrant its general acceptance   The accepted indications for the cisternal administration of antimeningococcic serum at the present time are (a) where the spinal route is unsatisfactory, (b) where spinal subarachnoid block is present or suspected

Naturally, where blockage exists at the foramina of Magendie and Luschka, serum injected into the cisterna may not reach the ventricles   Unfortunately, this is the commonest site of obstruction in meningitis   Apparently it occurs in about 1 5 per cent of cases[21, 22, 23] of meningococcic meningitis   If this complication presents itself, the maneuver of Cobb[7] should first be resorted to, in the hope of overcoming the obstruction   If this fails, ventricular puncture for the purpose of introducing serum above the point of obstruction should be considered

In the later stages of meningitis, where a tendency toward chronicity appears, the use of vaccine is often helpful [6] To summarize the present-day teaching with respect to the treatment of meningococcic infection we may say

(a) If seen in the septicemic stage before meningeal involvement has occurred, give a potent polyvalent antimeningococcic serum by vein, due precautions against anaphylactic shock being taken

(b) In the acute meningitic stage, give the serum intraspinally, using cisternal puncture if necessary, and continue giving it, so long as the clinical or bacteriologic evidence points to active

infection If one make of serum does not lead to improvement, change to another make

(c) If evidences of block appear take whatever measures may be necessary to introduce the serum on both sides of the obstruction

(d) If the condition runs into a subacute or chronic stage use a vaccine, autogenous if possible

(e) If localized abscess formation occurs, surgical drainage is indicated

Summary —A case is presented of meningococcic meningitis with subsequent staphylococcic infection, low spinal subarachnoid block, and abscess formation The patient made a complete recovery following the evacuation of an abscess about the cauda equina within the dural sac. This is believed to be the second case of its kind in the literature

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CLINIC OF DR JEFFERSON H CLARK

SAMARITAN HOSPITAL

DIFFERENTIAL DIAGNOSIS OF A CASE OF ENDOCARDITIS

THE following case has been selected to show the difficulties that may be encountered in making a positive "type" diagnosis, even when one has the clinical history, physical examination and autopsy findings for comparison

E H , age thirteen years

Entered the hospital 12/20/28

Died 2/4/29

Working Diagnosis —Rheumatic endocarditis

Final Diagnosis —Rheumatic endocarditis with valvular insufficiency

Chief Complaint —Recurrent attacks of pain in joints, dyspnea, palpitation

Past History —Six years ago, both knee- and ankle joints became swollen, red, and painful   This was associated with fever but no chills   Remained in bed for six weeks   Two months later, he was told he had cardiac involvement   Similar attacks recurred each year   For the past five years, he has been seen once a week in the cardiac clinic when his condition permitted   A year ago, he was suddenly awakened by a severe pain in the region of the heart, with difficulty in breathing   An ice-bag afforded relief   He had frequent attacks of tonsillitis prior to a tonsillectomy three years ago   He had also been treated with Small's serum (S C A) and antigen with no improvement

Physical examination on admission showed a poorly nourished boy

Heart Apex beat was in sixth interspace to the left of the midclavicular line, very diffuse in character Left border of heart extended to the left of the midclavicular line, the right at the parasternal line Muscle tone was poor Heart was markedly overactive and irregular at times There was a presystolic thrill over the mitral area, and a mitral systolic and aortic diastolic murmur Blood-pressure 90/65

Liver Reached to just below the costal margin Spleen was not palpable Urine on admission was negative Blood showed a secondary anemia with 12,250 W B C Polymorphonuclears 86 per cent Blood-culture on admission showed staphylococcus

Course in Hospital —The patient ran a very irregular temperature, received antistreptococcic serum and sodium cacodylate intravenously on two or three occasions, and later in his hospital stay Sherman's mixed vaccine almost every day

12/19/28 Fine granular casts appeared in the urine, and many pus cells, but no red cells

The secondary anemia increased The W B C fell to 8650 with 80 per cent polymorphonuclears

1/18/29 W B C fell to 6000 with 32 per cent polys

1/19/29 Heart clinic stated that "case clinically stands between ordinary rheumatic carditis and subacute bacterial endocarditis Spleen slightly enlarged No petechiæ noted "

1/26/29 Blood-culture yielded staphylococcus

Pulse-rate gradually increased in rate Temperature still persisted but with greater daily fluctuations, suggesting sepsis Two days before death temperature dropped to subnormal, pulse rose to around 150 per minute and respirations increased to 50 to 60

Autopsy —There was a small raised hemorrhagic spot with yellowish center on the sole of the left foot The lungs were practically negative The pericardium contained 3 to 400 c c of clear fluid, with a very occasional thin strand of fibrin All cavities of the heart were markedly dilated The posterior surface of the left auricle showed an area about 5 cm square, covered with irregularly sized, relatively small, apparently

smooth, pedunculated, and sessile vegetations, spreading from the mitral valve   Similar vegetations were on the chordæ tendinæ, many of which were broken   They appeared to be covered with endothelium   The endocardial surface of the left auricle was definitely thickened   The mitral valve was thickened and shortened   The aortic valve showed warty pedunculated growths   The spleen showed fresh and healed infarcts and was definitely increased in size

Both kidneys showed fresh and old infarcts

Liver was congested

Discussion —Let us now consider in more detail the various positive and negative findings in the history, physical examination and autopsy of this patient, and attempt to arrive at a positive diagnosis

First the history—there is a definite history of tonsillitis which, as you know, is one of the commoner findings in the triad—tonsillitis, chorea, and rheumatism   There is also a history of swollen, reddened, painful joints   However, a glance at the key to diagnosis in endocarditis will show that this may also occur in the subacute and acute bacterial as well as rheumatic endocarditis

There is also a history of a sudden sharp pain in the region of the precordium, which was relieved by an ice-bag   This may have been a pericarditis   Subsequent history neither corroborates nor refutes the possibility

The autopsy recorded a serous pericarditis of only moderate degree, with no evidences of a previous attack   Possibly the fluid found at postmortem was more of a terminal condition and should not influence us too much in arriving at a diagnosis, although the character would argue for a rheumatic or indeterminate type, rather than an acute bacterial, when the fluid is more commonly purulent in character

Purpuric spots or gross or microscopic emboli—no history was obtainable of either purpuric spots or the so-called "fibroid nodules" occurring in rheumatic endocarditis   Neither was there a history of Osler's tender nodes or Janeway's lesions, except the one noted on the sole of the left foot at autopsy

So that from the clinical standpoint, embolic phenomena were of no value in diagnosis Necropsy, however, gives very definite positive evidence in favor of the gross emboli which are found in acute or subacute bacterial endocarditis, for both old and new infarcts were found in the spleen and kidneys The amount of contraction which had occurred in the infarct in the right kidney particularly would indicate the lapse of several months at least from the primary damage The histopathology of the kidney shows the occlusion of some of the glomerular tufts, suggesting beginning Baehr-Lohlein lesions, and corresponds to the type of embolic lesion encountered in a subacute bacterial endocarditis

The heart—the type of vegetation encountered on the mitral and aortic valves and the posterior surface of the left auricle, conformed rather closely to those ordinarily encountered in subacute bacterial endocarditis First they were much more extensive than the pearly white, uniform-sized endothelial covered vegetations, limited to the line of closure of the valves in rheumatic endocarditis In this case, they extended from the chordæ tendinæ to well up on the surface of the left auricle They were not of uniform size, but were not extremely bulky Histologic examination showed them to contain bacteria, and the muscle in the immediate vicinity showed an acute inflammatory reaction with infiltration with polymorphonuclear leukocytes This rather argues for an acute bacterial endocarditis, but is not supported by the presence of ulceration

The changes in the heart muscle itself are more characteristic of an acute condition than a subacute, for while no Bracht Wachter bodies were found, there were numerous areas of interstitial infiltration with polymorphonuclear leukocytes No Aschoff bodies were found, but then, whatever the type of endocarditis, it is not an acute rheumatic, and although this present condition may have localized on a valve already damaged by a rheumatic process which is so common in both acute and subacute bacterial endocarditis (see chart), the Aschoff bodies present during the acute stage would have undergone resolution and have left only a scar in the interstitial tissue of the myo-

cardium, practically impossible of identification now as a healed Aschoff body

Key to Diagnosis in Endocarditis

	Rheumatic	Acute Bacterial	Subacute Bacterial	Indeterminate
Joints	Reddened	Reddened	None	Maybe
Erythema Nodosum	Painless Subcutaneous Fibroid Nodules	No	No	Maybe
Janeway Lesion	No	Yes	No	Maybe
Osler tender Node	No	No	Yes	No
Pericarditis	Serous	Often purulent	No	Maybe
Blood Culture	Negative	Streptococcus Pneumococcus Staph Gon	Strep Influenza	No Bacteria
Vegetation	same age (small) line of closure No acute reaction	Largest different ages acute with necrosis Purulent & Bact.	Large fibrosis with calcification	Flatter Larger
Ulceration	None	Yes with abscess	None	No
Extent	Line of closure healthy valve	Auricle Chordae Tendinae Congenital or diseased valves	Auricle Chordae Tendinae	Tricuspid 55%
Muscle	Aschoff	Acute Abscess Polys	Bracht Wachter	No Aschoff or Bracht. Wachter
Kidney	Negative	Infarct	Bant free Bashr Löhlein glomerular nephritis	Negative
Emboli	None	Retinal hemorrhage	Retinal hemorrhages common	No

Fig 172

Bacteriology—this very important feature of diagnosis is not so much negative in our case, as it is negligent We probably learn more from our mistakes and acts of wrong doing than from our acts of right doing, and in this particular case, mistakes were made by both the clinical and pathologic departments In the first place, a mistake was made by the clinicians in not checking up on the positive staphylococcus blood culture a third time The original cultures, I believe, were made more as a routine measure than for purposes of diagnosis, because the boy had

been diagnosed a rheumatic endocarditis before admission   But
the staphylococcus recovered twice from a blood-culture should
have been confirmed as an organism in the circulating blood, or
else proved to be a skin contamination by subsequent blood-
culture   We are in the habit of considering growths of staph-
ylococcus as skin contaminations unless repeatedly obtained by
blood-culture   In view of the postmortem findings, this might
well have been an inhabitant of the blood-stream   The patho-
logic department made an even more serious error in not cul-
turing the vegetations at postmortem   The reasons for not doing
so, were, first, the clinical diagnosis, second, the type of vege-
tation, for at autopsy these seemed to be covered by endo-
thelium and consequently not active from a bacterial standpoint,
and, third, the lack of asepsis in opening the heart   None of
these reasons however, excuses our neglect in attempting to
obtain bacteriologic evidence of the cause of the vegetations

Summarizing then our points for a definite diagnosis, we
have the following

1 Decided positive evidence of gross embolic lesions as indi-
cated by the infarcts in spleen and kidneys

2 Extensive vegetations resembling grossly the lesions seen
in subacute bacterial endocarditis, but microscopically conform-
ing to an acute bacterial type

3 Absence of Aschoff and Bracht Wachter bodies in the
heart muscle, but an infiltration with polymorphonuclear
leukocytes

4 Staphylococci recovered in blood-culture at intervals of
three months, although not confirmed at autopsy

5 A rather typical history of rheumatic endocarditis prior to
entrance to the hospital

All these seem to point to an acute bacterial endocarditis
engrafted on an old rheumatic lesion

CLINIC OF DRS M G WOHL and J H CLARK

SAMARITAN HOSPITAL

CLINICOPATHOLOGIC CONFERENCE

DR M G WOHL Mr L , age forty-eight years, came into the hospital with a chief complaint of "yellowing of the skin."

There is nothing of interest in his family history except that his mother died of tuberculosis at the age of forty-four years

Present Illness —Two years ago, the patient noticed a gen eral discoloration of the skin, which commenced slowly It was distributed all over the body, and the yellowing of the skin was intermittent The patient had no pain, but he says his strength became poorer and he began to complain of a tired and weak feeling after doing even very light work His appetite was good He had no gastric upsets but suffered from obstipation, and his stools were of gray color He also states that he had to get up at night to urinate two or three times, the urine having a green ish tinge The patient has lost 10 pounds in weight since his illness began

Past History —He had mumps, measles, in childhood, and typhoid fever in adult life

Habits —He uses tobacco in the form of cigarettes and smokes quite heavily Alcohol He has been in the habit of drinking for many years, averaging about 3 quarts a week How ever, he has not drunk within the last few years

Physical Examination —Patient presents a marked jaundice over the entire body Eyes Sclerae are jaundiced

Heart The apex beat was diffuse and not palpable Heart sounds feeble, distant, with the greatest intensity at the sixth interspace, 2 cm to the left of the midclavicular line, the right

border at right parasternal line   The lungs revealed many moist râles posteriorly at the bases, pleuritic friction rub heard in the right axillary space

Abdomen   No tenderness on palpation   Liver enlarged, being 6 cm below the right costal margin   The surface of liver was smooth   The spleen was palpable

Extremities   No edema   There was a marked discoloration on the inner aspect of both the tibiæ   He also had a marked clubbing of the fingers of both hands

When the patient came into the hospital his temperature varied between 96 8° and 99° F   His pulse varied between 60 and 70   His respirations were 20

Laboratory Findings —The urine was consistently low in specific gravity, varying between 1 008 to 1 010 and on one occasion was 1 020   Albumen was positive   Bile pigments were present   Casts were found   The blood chemistry showed the non-protein nitrogen of 25 8 mg , uric acid 3 1, and creatinin 1 06 The van den Bergh gave a direct positive test   The icterus index was 55 units   The blood showed a hemoglobin of 79 to 80 per cent   and the red cells varied between 3,800,000 to 4,000,000 The white blood-count was 7900 with 72 polymorphonuclear leukocytes, 21 per cent small lymphocytes, and 7 per cent large lymphocytes   The stool gave a positive reaction for occult blood An Ewald test-meal showed hydrochloric acid of 52, and total acidity of 68   The test for occult blood was positive

The patient also had a biliary drainage, and the important point disclosed was that bile was present

Diagnosis —Biliary cirrhosis (Hanot?)

He was operated on by Dr Babcock, and the following notes were made on the operative record   "The liver is dark greenish brown in color, right lobe extending down one fingerbreadth below right costal margin   Left lobe is at the level of the navel The spleen is 5 cm below the ninth rib   The surface is smooth, and the edges rounded   The gall-bladder is dense and contained thick bile   The lower surface of the liver is hob-nailed The left kidney is larger than normal, and there are cysts on the surface   There is some excessive peritoneal fluid of a greenish

tinge." A cholecysgastrostomy was done The patient made an uneventful recovery from his operation and went home.

Four months later, he was readmitted to the hospital, presenting still the marked jaundice, but in addition, he developed a marked enlargement of the abdomen Several tappings were made, averaging one every two weeks The patient continued to go from bad to worse and died

Let us analyze this case The important point is his marked jaundice, a jaundice that lasted for two years The jaundice was not accompanied by pain and the stool was gray in color One would ask the question "What kind of jaundice did the patient have?" We discussed it at our last conference Jaundice may be due to excessive bile formation, or the so-called "hematogenous jaundice' Is this a hematogenous jaundice? In hematogenous jaundice the stool is usually brown in color In addition, the urine shows no bile but urobilin The blood gives an indirect van den Bergh reaction that is, if one takes blood serum and mixes it with the Ehrlich diazo reagent, no red color will develop unless one first adds alcohol to it

In this patient, all these manifestations were absent Therefore, one can rule out hematogenous jaundice

There is another kind of jaundice described by the Germans as "paracholic jaundice,' and what we designate as catarrhal jaundice, but as mentioned in the history the patient did not have any gastro intestinal symptoms In paracholic or the so-called "catarrhal jaundice," they have gastro-intestinal symptoms The patient usually states that he ate something that "upset his stomach" and later he develops jaundice, but as a rule, it does not last very long The jaundice usually lasts for about two to six weeks The patient as a rule gets well, or he may, according to the German teaching, develop an acute yellow atrophy of the liver In this patient, all these manifestations were likewise absent Therefore, it is not a paracholic jaundice

The only other type of jaundice to be considered, is the obstructive type This could be either extrahepatic or intrahepatic, or within the lumen of the duodenum or common bile-

duct   The extrahepatic obstruction may be due to a tumor of the pancreas pressing upon the ducts from the outside

The very fact that this man did not have cachexia nor pancreatic insufficiency, such as a butter-like stool, glycosuria, also the presence of bile in the duodenum obtained by duodenal drainage, would almost rule out the extrahepatic cause for jaundice

So, the next thing to consider is either an obstruction within the lumen of the duodenum, or within the common bile-duct The most common cause of these types of obstruction is a stone In the presence of a stone, the patient usually gives a history of a gall-bladder colic

Second, as a rule, in obstructive jaundice due to stone, there is pain, chill, and fever and the jaundice is not as marked as in the case of this patient

The obstruction could also be due to an old ulcer of the duodenum with a scar formation which would obliterate the duct at the entrance into the papilla of Vater   The negative gastric history, the almost normal acidity and the x-ray findings have ruled this out

The x-ray report was as follows   "The stomach does not show any organic pathology   There is a slight five-hour gastric residue, and the cap fills normally   Appendix is long and dilated in its distal portion   The liver area is enlarged "

Now, as to the intrahepatic cause of obstruction   This is due to anything that will cause blocking within the small bile capillaries, or in other words, a radicular cholangitis generally known as biliary cirrhosis of the liver   There are several forms of cirrhosis of the liver   One form that is well known, is the Laennec or so-called "alcoholic cirrhosis of the liver "   It is true that in a number of patients there is a history of the use of alcohol, yet there are individuals with cirrhosis of the liver in whom the use of alcohol is absolutely denied   Therefore, the assumption that the excessive use of alcohol is the sole cause of this type of cirrhosis of the liver is not borne out by clinical and neither by experimental facts   There must be other factors besides the use of alcohol which are responsible for the condition   It is interesting to note that people with this type of cirrhosis of the liver, are

usually stigmatized people. They have an abnormal distribution of hair. You hardly ever see a patient with cirrhosis of the liver who has, if he be a man, a normal growth of hair on the chest. Usually it is absent or scarce in growth. The axillæ also show lack of hair, or a very scant growth. On the other hand, the hair on the head and the beard is very heavy. In other words, this type of individual has a "degenerative constitution" (inferior constitution).

In Laennec cirrhosis there is primarily a proliferation of connective tissue which has a tendency to shrink. Therefore the liver is small.

There is another form of cirrhosis of the liver where the overgrowth of connective tissue does not result in shrinkage. In this type of cirrhosis, the liver is usually large and in addition, the connective tissue has a tendency to localize around the bile capillaries. In the Laennec cirrhosis, the connective tissue predominates around the portal system, and because of this, the patient has early portal symptoms. He also has a congested spleen, and a large spleen usually accompanies this condition. The patient also has symptoms referable to the gastro-intestinal tract. Then again there is a dilatation of the superficial vessels either around the navel, or very often, there may be dilated veins in the lumbar region. One can best demonstrate the presence of these veins by telling the patient to stand up and bear down as if going to stool. Jaundice is not prominent in this type of cirrhosis. It is true that the jaundice may appear, but usually only late in the disease.

With proliferation of the connective tissue the parenchyma becomes degenerated, but nature makes up for this by the formation of new liver lobules. However, the new lobules do not function in the same manner as the old ones. The histologic picture of the new lobule is different. While in the normal liver, the main vein is located centrally, in the newly formed lobules the vein may be located anywhere. You may find the lobules with the vein at the periphery, but hardly ever in the center as in a normal liver. Because of this, the liver does not function normally, in spite of the newly formed lobules, and therefore, in

addition to the portal circulatory disturbance, the patient may also manifest symptoms of liver insufficiency

From the symptoms and the history our patient presented, we can therefore rule out Laennec's cirrhosis

There is another form of cirrhosis in which the primary factor is an obstruction in the small bile capillaries   This type of obstruction may be due to inflammation within the capillaries with desquamation of cells, and the degeneration of the adjacent liver cells with proliferation of connective tissue   The connective tissue may be either around or within the liver lobules proper   This is known as biliary cirrhosis   This form of cirrhosis may be seen in people who have a pathologic gall-bladder   We used to believe that a patient with a gall-bladder disease, cholecystitis, or cholelithiasis, had a disease entity limited to the gall-bladder   It is now known that a number of such people have an associated hepatitis   When pieces of liver, excised during gall-bladder operation, are examined microscopically, one finds evidence of inflammation   One can readily see that if the condition lasts long enough, instead of the round-cell infiltration, there will also be connective-tissue formation   Indeed, in chronic gall-bladder disease, one may find associated biliary cirrhosis

Again, various toxins may account for this form of cirrhosis   A former disease, in which the liver was damaged, is an important factor   Typhoid fever in the history of this patient is of importance   There are certain diseases which are accompanied by the presence of urobilin in the urine   Urobilin in the urine means an insufficiency of liver function   I believe it is one of the best tests we have for estimation of liver function   In typhoid fever, very commonly, urobilin is found in the urine   In gall-bladder disease, cholecystitis, and cholelithiasis, and in malaria, there is also an urobilinuria   It indicates that these diseases damage the liver   We find that people developing cirrhosis of the liver, give a history of a former disease that was accompanied by urobilinuria   Such a disease causes a local predisposition for whatever factor might later in life cause cirrhosis of the liver   Alcohol likely played an additional predisposing rôle in the cirrhosis of the liver of this patient

In biliary cirrhosis, the primary symptom is jaundice such as this patient had In addition to the jaundice, the patient had a gray-colored stool The jaundice is intermittent as was the case in our patient, and the blood gives the direct van den Bergh test. Our patient had a positive direct van den Bergh and an icterus index of 55

The patient complained of constipation This may be explained by the absence of bile in the intestines The bile is a great stimulator of peristalsis of the bowel The fluid in the abdomen, though very small in amount as described by Dr Babcock in his operative record, was green in color Whenever one finds serous fluid, or when the urine is of green color, one is pretty sure that there is some form of liver insufficiency The spleen is large in biliary cirrhosis

There is an interesting observation in this patient He had clubbing of the fingers, which, as you know, is due to a local cyanosis It is a common finding in pulmonary conditions such as bronchiectasis or carcinoma of a bronchus One may find a unilateral clubbing in mediastinal tumors Then, of course, one sees it in congenital heart disease

This patient showed none of these diseases, and yet he had clubbing of the fingers People that have a protracted jaundice, have fingers that look like clubbed fingers, but this is not true hypertrophic osteo-arthropathy The apparent clubbing is due to an increase in the subcutaneous tissue

I want to mention another type of cirrhosis which is not common—the so called "Hanot's cirrhosis" This disease is very rare According to Chvostek, in Austria not a single case has been reported In this country, men of wide clinical experience are still looking for a case of Hanot's cirrhosis

As to the ascites that our patient developed, the connective tissue may encroach also on the portal circulation in biliary cirrhosis Hence the ascites in this case.

It is rare for one to see a clear-cut case of biliary cirrhosis with an absence of symptoms referable to the portal circulation We would therefore expect to find in this man

First A liver that is characteristic of biliary cirrhosis and

a large spleen   Secondly   He complained of nocturia, and had
to get up several times at night to urinate   This is a symptom
which is common in kidney disease   We would expect to find,
therefore, kidneys showing chronic nephritis   He also had albu-
men and casts in the urine which would lead us to suspect chronic
nephritis   However, albuminuria may be due to the presence
of bile   Finally   From the physical findings, we would expect to
find a dilated heart and evidences of a pleuritis and pulmonary
congestion

DR CLARK   Dr Wohl has certainly developed the diagnosis
in this case as though he had actually seen the postmortem   Yet,
I know he did not, because it was performed some months
before he came here   I will pass around specimens of the liver
and spleen while we take up the pathologic findings at post-
mortem

As Dr Wohl expressed it from a clinical standpoint, first he
diagnosed biliary cirrhosis of an obstructive and infectious type
At autopsy, the liver was not enlarged   It was much smaller
than normal and hob-nailed in appearance and of a brownish-
green color   It cut with greatly increased resistance, and the
cut surface, as you can see in the specimen, shows strands of
fibrous connective-tissue running through the substance of the
liver, isolating small lobes of liver cells of varying sizes   (In
this specimen, the actual color has been lost to some extent and
a large amount of the green color that was present then has been
dissipated in the preserving fluid)

Microscopically, the liver showed an extreme irregularity in
its architecture   As Dr Wohl illustrated on the blackboard,
there was no definite relationship between the central vein and
the liver lobule   There was a connective-tissue overgrowth
outside of the lobule, and also penetrating inside the lobule
This connective-tissue overgrowth varied in its amount in dif-
ferent areas in the liver   In some places, there were extremely
wide areas, and in other places the strands of connective tissue
were relatively thin   However, they showed in general, an
intense round-cell infiltration   In the areas of connective tissue
that were larger in amount, there also was a suggestion of begin-

ning proliferation of the bile capillaries, apparently an effort on the part of the liver to hitch up bile capillaries with newly formed liver cells

As you know, connective tissue has the general characteristic of contraction with age   From the time this patient was operated on, until we got the postmortem, five months elapsed which allowed contraction of the connective tissue and the consequent decrease in the size of the liver   So, while it is very easy to see that early in his illness he may have had a true biliary cirrhosis, with an enlarged liver, later, with the contraction of the fibrous tissue, the portal circulation was involved, and constriction of the blood vessels resulted in ascites

The individual also had about 3 or 4 quarts of clear fluid in the abdominal cavity   This, however, was not bile stained at postmortem   I might say that the cholecystogastrostomy was shown at postmortem to have functioned prior to death   One could insert the tip of the little finger through the opening between the stomach and the gall bladder

However, we did find deep in the cystic and common duct, small gravel particles of inspissated bile   Whether this might primarily have had something to do with the production of jaundice I am not prepared to state   We could still, however, get probes through the common duct into the duodenum

A kidney condition is mentioned because of the urinary findings   At autopsy, the kidneys were slightly larger than normal and somewhat softer in consistency   Areas were encountered in the kidney parenchyma pale yellow in color, not sharply circumscribed but softer in consistency than the surrounding tissue, with the softness located in the center of these yellow areas   On section through these areas, occasional ones showed very distinct softening similar to pus

Microscopic examination of the kidney showed an irregular increase in interstitial tissue and slight increase in the connective tissue around the glomerulæ   Scattered throughout the medulla and cortex were groups of lymphocytes and pus cells, indicating a pyelonephritis and early chronic interstitial nephritis

Dilatation of the heart was mentioned as a possibility or

probable diagnosis with pigmentation as a result of his jaundice
This man's heart was smaller than normal, relatively smaller in
comparison to the size of the body   There was a very small
amount of fat present   The heart muscle itself was extremely
dark brown in color suggesting a beginning brown atrophy

The only other finding of importance at postmortem, apart
from the enlarged spleen which you will see as it is passed
around, was a bronchopneumonia present in both lungs   In
addition to this bronchopneumonia, there were areas in which
the alveolæ were filled with round cells

(One thing I forgot to mention was a subacute peritonitis
in which the coils of the intestine were matted together with
adhesions quite fresh, although there was no evidence of an
acute suppurative condition   The intestines themselves seemed
slightly water-logged and thickened)

Our diagnosis in this case from the standpoint of pathology,
was   "Obstructive biliary cirrhosis, infectious in type, chronic
splenitis, brown atrophy of the heart, bronchopneumonia, pyelo-
nephritis and ascites "

QUESTIONS BY STUDENTS —Was there any evidence of tuber-
culosis or lymphadenitis?   None was found postmortem   How-
ever, we failed to examine minutely the seminal vesicles and
prostate, although it is well known cirrhosis and tuberculosis are
frequently associated (Dr Clark)

What is the length of time and what is the prognosis of biliary
cirrhosis?   From three to five years, and they usually die from an
intercurrent condition

How do you explain the presence of occult blood in the stool?
By the hemorrhagic diathesis that accompanies jaundice and the
portal congestion

Was any bile obtainable from the patient at any time in
biliary drainage?   Yes, and its presence helped to rule out out-
side pressure on the common duct (Dr Wohl)

CLINIC OF DRS JAMES E TALLEY AND GEORGE C GRIFFITH

PRESBYTERIAN HOSPITAL

A DISCUSSION OF SIX CASES OF AGRANULOCYTOSIS

UNTIL July 1, 1929, 92 cases of agranulocytosis or agranulo cytic angina have been reported   The purpose of this discussion is to present 6 cases of agranulocytosis, two of which conform clinically to the picture described by Schultz[1] in 1922   A short résumé of this disease entity may be in order

The clinical features of agranulocytic angina are distinct and strikingly characteristic. The majority of the reported cases occurred in middle aged women, about half of which were debilitated by some chronic illness   The onset was acute, although short or long illnesses may precede the onset   There was soreness of the throat, generalized malaise, dysphagia, extreme prostration, chills, and fever   Fever was early, and persisted in all of the cases   In 58 per cent of the 43 cases analyzed by Kastlin, jaundice was present   The oral cavity and occasionally the lower parts of the gastro intestinal tract, stomach, duodenum, ileum, colon, rectum, and anus, showed ulcerative and necrotic processes   The course of the disease was acute, death occurring in the vast majority of patients in from three to seven days, while a few patients have lingered from four to six weeks   Recently, however, M Call[3] and Blauton[4] each reported a case with recovery   Convalescence in these cases was greatly prolonged

The etiologic agent is unknown   From the oral lesions Viacent's spirochetes and fusiform bacilli, diphtheria bacillus, Bacillus pyocyaneus,[5] staphylococci,[6] pneumococci, and strepto cocci of different types have been isolated   In the majority of

the cases the blood-stream remained sterile, but the Streptococcus hemolyticus, S viridans, pneumococcus, Bacillus coli, and B pyocyaneus have been isolated

The blood-picture deserves review, as it is most striking, and usually is the lead to the diagnosis   In all cases there was a definite leukopenia, *i e*, the white blood-cells fell to 1000 cells per cubic millimeter or less   The granulocytes or polymorpho-nuclear cells were either greatly reduced in number or absent The lymphocytes were present in normal numbers, or actually increased so that a differential count may show 100 per cent lymphocytes

The pathologic findings were those of a severe septicemia with the lungs showing a confluent bronchopneumonia   The liver and spleen were enlarged   The pleura, endocardium, and lymph-nodes showed small hemorrhages, while the liver, spleen, lymph-nodes, and kidneys showed bacterial emboli with areas of necrosis   The tonsils, pharynx, stomach, and intestines may show superficial necrotic foci   In the bone-marrow the granular cells were decreased and the lymphocytes were left prominent by contrast   The pathologic physiology was presumably a granulocytic aplasia

Case I —C T F , fifty-six years of age, lived a very active life, and was considered a very healthy male   During the past three weeks the patient had a chill every third day, the cause of which was unknown   It was thought that he had had an infectious arthritis, involving the shoulders and phalangeal joints, for one year   Two weeks prior to admission he had a lower left molar tooth extracted   One day before admission he had a chill, temperature of 101° F, pulse of 120, and respirations of 20 At 5 00 P M his condition was good, except for a chill which had lasted about one hour   At 6 00 P M he had aching in all parts of his body, and the temperature had risen to 103° F The history was otherwise negative

Physical examination showed the eyes, ears, nose, and throat to be negative for any pathology or acute inflammation   The tonsils were small, cryptic, and not markedly inflamed   There

were some palpable glands in the middle portion of the anterior cervical chain On the next day, November 12, 1926, at 8 00 A M his temperature was 103° F, the pulse still 120 No other physical findings developed from the previous day On November 12, 1926, at 4 00 P M, the patient developed a swelling in the left side of the neck at the angle of the jaw, this was hard, indurated, and measured 2 by 3 cm At 8 00 P M he had a temperature of 104° F, became very toxic, and at that time was sent to the hospital

On admission to the hospital the physical examination was entirely negative, except that there was this hard, indurated tender mass in the left side of the neck The patient was seen by a surgeon and a laryngologist, who decided that an exploratory incision should be made into the region of the swelling This was made under local anesthesia, and the incision extended under the deep fascia, but no pus was found The patient gradually grew worse Two leukocyte counts were made on admission of the patient to the hospital, both showed a leukopenia of 720 A differential count was made, which revealed 100 per cent lymphocytes The blood-culture, which was taken on admission, was positive for Streptococcus hemolyticus The patient died within twelve hours after admission A postmortem examination was not obtained

Case II—A V T, fifty years of age, white female house wife was well until five days previous to admission, when she received a small cut in the palm of her right hand A slight infection followed She immediately consulted her local physician. He did not find her condition alarming until the day of admission, when he advised her to seek hospitalization

Upon admission, the patient gave the appearance of an acutely ill woman in moderate shock and semiconsciousness Her skin was cold and clammy, the pulse very feeble, with a rate of 100 Her temperature, upon leaving home to come to the hospital, was 102° F, and on admission was 97 4° F, the blood pressure was 66/40 The index finger of the right hand was cold and cyanotic The entire right hand was slightly cyanotic

There appeared to be an inflammatory reaction extending along the course of the veins of the forearm to the region of the elbow The epitrochlear and axillary lymph-nodes were not enlarged The veins in the antecubital space were slightly inflamed The leukocytic count was immediately made, showing 1250 cells, with a differential count of 100 per cent lymphocytes Within three hours the entire hand and arm became more blue, and large vesicles formed Smears were taken to determine the infecting organism Although the smears were negative, it was thought advisable to give Bacillus welchii serum Forty c c were given intravenously The patient continued to grow rapidly worse, and died six hours after admission The blood-culture was sterile The leukocyte count was repeated, and found to be 1000, of which 100 per cent were lymphocytes

Case III —K S , sixty-eight years old, white, female house-wife, had been in good health until one day before admission, when she began to feel weak, lost her appetite, developed a slight sore throat, and that evening had a chill When she awakened the next morning the throat was somewhat sore, and she vomited several times She became progressively more toxic and was sent to the hospital The patient had had the usual childhood diseases, occasional sore throat, and pneumonia two years previously She also had diabetes, which was well con-trolled at the time of this illness by 10 units of insulin daily

Physical examination showed a white female, who was very stuporous, and when she did speak, considerable effort was re-quired The scalp, ears, eyes, and nose were entirely negative The teeth were all removed, the tongue was slightly dry The throat showed nothing more than a dusky redness extending over the anterior pillars, which were slightly edematous The right tonsil was somewhat enlarged, with a few yellowish spots upon it There were a few submaxillary lymph-nodes, palpable, but not tender The neck was negative, and the lungs were negative throughout The heart was not enlarged, sounds were well heard, and the heart-rate was 126 The blood-pressure was not taken The patient had two healed furuncles on her

back A tentative diagnosis of acute streptococcic sore throat was made An immediate blood-count was made, which showed only two cells in the entire counting chamber Differential, made at that time, showed ten cells, nine of which were lymphocytes A blood-count made the following day showed 600 leukocytes, with a differential of 100 per cent lymphocytes The blood-sugar on admission was 236 mg per 100 c c, and the plasma CO_2 was 52 volumes per cent The blood sugar the following day showed 168 mg per 100 c c Smears from the throat showed a hemolytic streptococcus infection The blood culture was positive for hemolytic streptococcus infection The patient died eighteen hours after admission, and the final diagnosis was that of agranulocytic angina

Case IV —B H , sixty years of age, white female, was admitted April 9, 1929 at 2 00 p m , complaining only of pain in her right ear She had had a cold in her head for four weeks, and had an abscess in her external auditory canal, which was opened the day of admission She had a chilly sensation since the incision of the abscess There was no mastoid tenderness and no dropping of the superior canal wall The throat was congested and the opinion was given that the ear was not responsible for the patient's temperature of 102° F , pulse of 124, and respiration, 25 The next day the pharynx was very much congested and edematous The opinion was given that a very acutely inflamed sore throat was probably the cause of the high temperature The following day the pharyngeal and tonsil regions were very dry, and showed evidences of some membranous deposits, but not the usual picture seen in agranulocytic angina The furuncle of the external auditory canal drained well, and there was no mastoid tenderness.

Physical examination of the chest showed an area the size of 3 cm at the angle of the left scapula where there was slight bronchovesicular breathing There were no other signs in the chest The leukocyte count at this time was 600, with 80 per cent lymphocytes and 20 per cent. monocytes There was only

one polymorphonuclear leukocyte found on the entire smear
The patient became more toxic, the pulse became imperceptible,
and the patient died thirty-six hours after admission   The blood-
sugar was 139 mg per 100 c c , the blood-urea nitrogen 19 mg
per 100 c c   A blood-culture was negative   A throat-culture
was not made

Case V —R P , thirty-six years of age, colored female, ad-
mitted to the hospital because of weakness, fever, vomiting, and
a skin rash   She had not been well for several months   A
blood Wassermann had been taken and found to be positive
on June 4, 1928   She was given 0 6 gram of neo-arsphenamin
intravenously and had no reaction   One week later she was
given a second injection of 0 75 gram of neo-arsphenamin, and
that evening she became very weak, had several chills, and a
very severe headache   The next day she continued with fever,
headache, and weakness, and the third day a physician was
called, who found her temperature to be 103° F   She still
remained quite ill with nausea and vomiting, and this continued
for six days, when she was admitted to the hospital   Although
the day previously she had been seen by a member of the City
Board of Health because she had a rash, it proved not to be
that of scarlet fever, but was that of a toxic dermatitis

On admission the patient was acutely ill, face edematous, lips
and tongue were dry   The ears and nose were negative, the
teeth in good condition, the tonsils evidently diseased, and
over the posterior pharyngeal wall there was a thick muco-
purulent discharge   The glands of the left cervical chain were
enlarged, the lungs were entirely clear, the heart showed no
pathology, and the blood-pressure was 125/75   The abdomen
could not be examined carefully, because the patient was unable
to release the tense abdominal muscles   Over the entire surface
of both arms there seemed to be an erythematous macular rash
which did not itch   The temperature on admission was 102° F ,
the pulse 124, and the respirations 38   The patient at this
time had a leukopenia of 3540 white cells, and the differential
count showed 46 per cent polymorphonuclears, 4 large lympho-

cytes, and 50 small lymphocytes   The urine showed many casts, both hyaline and light and dark granular   There was no arsenic found in the urine   A throat-culture showed a Staphylococcus aureus infection   The Widal's test for typhoid was negative   The leukopenia continued, with a rise in the large lymphocytes to 44 per cent, in small lymphocytes to 30 per cent, and in polymorphonuclears to only 36 per cent   Three days later jaundice increased, and the patient developed considerable twitching of the facial muscles   The icteric index rose to 76   The patient gradually grew weaker, jaundice became more marked, and the day previous to her death there were 1500 white cells, of which 10 per cent were polymorphonuclears, 35 per cent large lymphocytes, 51 per cent small lymphocytes, and 4 transitional cells   The final diagnosis was that of lues and arsenical hepatitis   The urine at all times continued to show a cloud of albumin, many hyaline and both light and dark granular casts, 50 to 75 white blood cells, and an occasional red blood-cell   Two blood-cultures were sterile

Case VI—J C, white, aged twenty five years, six weeks previous to admission to the hospital felt general soreness in his arms, back, and chest   Three days later he had sharp, shooting pains in the lumbar region, legs, and genitalia   The pain became so severe that one week after the onset he was sent to a hospital in a neighboring state, where he remained one week, and was treated by hypodermic injections   Three weeks after the onset he developed a slight fever with pain in the chest   x Ray of the chest was negative   The pain again returned in the thighs and legs   He was again taken to the same hospital, where he remained for three weeks, and was given two blood transfusions   He was transferred to his home where he remained a few days, and he then was admitted to the hospital where these studies were made   In his past history the patient had had scarlet fever, measles, and whooping cough severe influenza in 1918, and frequent sore throats throughout childhood   Six months prior to his last illness he had an attack of diphtheria, in which the glands of the neck became involved,

and had to be incised   He never recovered his health from the time he had diphtheria until the onset of the pains in his back five weeks prior to his admission to this hospital

Physical examination on admission showed a well-nourished, adult male   The skin had a marked yellow color and was moist and clammy   The mucous membranes were very pale   The patient was mentally clear and active   The eyes, ears, nose, and throat showed no pathology   The tongue was coated, the teeth were in fair condition, and the pharynx and tonsillar areas had a peculiar whitish appearance, which may have been due to anemia   Here there were a few congested blood-vessels which stood out distinctly   The tonsils were small and cryptic, from which pus could be expressed   The throat was not acutely inflamed   There was slight anterior cervical adenitis on both sides, and a small scar on the right side where the abscess had been drained six months previously   The lungs were clear on examination, the heart was not enlarged, there was a systolic mitral murmur, transmitted to the base and to the axilla, and the rhythm was regular   The blood-pressure was 100/48   The abdomen showed no distention, no tenderness or rigidity, and no organs were palpable   The patient had no symptoms whatever, except slight pain on defecation   On the third day after admission the temperature, which had been varying from 99° to 101° F , began to rise   The patient's neck became stiff, and an area of tenderness was found between the anterior border of the right trapezius muscle and the posterior border of the clavicle   This area was very tender, was red and hot to the touch, but there was no apparent swelling   A few hours after the onset of the rise in temperature the patient had a chill, and the temperature went up to 103° F   The physical examination was entirely negative except for the tenderness mentioned above

The patient became mentally sluggish, very weak, and the temperature continued to rise   On the fifth day after admission the area on the right side of his neck had become swollen, more red, and very warm   There was some pseudofluctuation or possibly true fluctuation over this area   The temperature rose to 105° F   The patient gradually became worse, and the pulse

more shallow and rapid, resulting in death six days after admission

The blood-count on admission showed 36 per cent hemoglobin, 2,120,000 red blood-cells, and 2800 white blood-cells, with 26 per cent of polymorphonuclears, 5 large lymphocytes, and 69 small lymphocytes   Three days later the leukocytes were 1500, with 5 per cent of polymorphonuclears, and 95 per cent small lymphocytes   On the fifth day the hemoglobin was 25 per cent , the red blood-cells 990,000, and the white blood cells 840, of which 100 per cent were lymphocytes   On the sixth day there were 1200 white blood-cells, with 2 polymorphonuclears, 3 large lymphocytes, and 95 per cent small lymphocytes   One month prior to his admission he had 90 per cent hemoglobin, 5,010,000 red blood cells, and 7000 leukocytes, with 31 per cent polymorphonuclears, 66 per cent. small lymphocytes, and 3 large lymphocytes   One week prior to admission to this hospital he had 3750 white blood-cells, of which 2 per cent were polymorphonuclears, and 98 per cent small lymphocytes   A throat-culture showed the Staphylococcus aureus   He had received two transfusions of 300 and 500 c c of citrated blood two weeks prior to admission   Blood-culture was sterile, blood urea nitrogen 25 mg , and blood sugar 125 mg   Consulting laryngologists reported no focus of infection in the nose or throat

Of the 6 cases presented, Case III and perhaps Case IV, should be considered as fitting into the disease entity of agranulocytic angina   Case III began very suddenly, Case IV moderately suddenly   In each there were chills and high fever, and both had only 600 leukocytes, with a total loss of the granular cells   Clinically Case III had an acute streptococcic sore throat, and the Streptococcus hemolyticus was recovered in pure culture   This micro-organism was found in the blood stream Case IV, however, had a short prodromal history of a nose and throat infection, involving her ear particularly   The blood-culture was negative

In Case I the origin of the infection appeared to be an infected tooth socket, the tooth having been extracted two weeks previously   The patient did not develop localizing signs until

the day before his death, however, he did have signs of an infection and possibly of septicemia for a week prior to his admission to the hospital   The blood-picture was that of an agranulocytosis   The socket and the blood-stream both yielded positive cultures of Streptococcus hemolyticus   This case would then appear to be one of an overwhelming virulent infection rather than a typical agranulocytic angina

Case II was a woman who had been in fairly good health until she scratched her hand five days before admission   Her physician noticed nothing unusual until the day of admission, when she showed signs of a very rapidly ascending gangrene of the hand and forearm   Her blood-picture was that of a typical granulocytopenia   This case also appeared to be that of an overwhelming infection rather than one of agranulocytic angina

Case V is similar to two other cases which have been reported in the past year, and accords with the well-known fact that arsenic leads to a leukopenia   The clinical course of chills and fever, some sore throat, albumin, white and red blood-cells, and casts in the urine lead one to suspect a superimposed infection   However, the throat-culture and blood-culture were negative   The blood-picture was that of a granulocytopenia, in which the granulocytes were not completely destroyed   If this case was more than one of an arsenical hepatitis, the origin and focus as well as the infecting organism could not be located

Case VI is that of a young man who six months previously had had diphtheria, and since that time had never been well   Six weeks prior to his admission to the hospital he was admitted to another hospital because of severe pain in the distribution of his sciatic nerves   Anemia and granulocytopenia gradually increased in severity over a period of six weeks   Finally a small abscess localized in the left supraclavicular space   The throat-culture and blood-cultures were negative   Unfortunately, a culture was not obtained from the abscess in the neck   The blood-picture near the end of his illness was that of a typical granulocytopenia with 840 white cells and 100 per cent lymphocytes